ELECTRONIC EFFECTS
IN AROMATIC SYSTEMS

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ABSTRACT

^{13}C NMR substituent chemical shifts for both ethenyl carbons in series of *meta* and *para* X- and XCH_2-substituted methyl cinnamates in six solvents have been obtained in an effort to investigate the influence of solvent on the inductive substituent constant σ_I. These data have been supplemented with ^{19}F NMR substituent chemical shifts for series of *meta*- and *para*- fluorobenzyl derivatives prepared in this study and with ^{13}C shifts for the styrenes and ^{19}F NMR data for the fluorobenzenes available from the literature. Modified σ^{meta} and σ_I values for use in the solvents ethanol, dimethylsulphoxide, acetone, deuterochloroform, carbon tetrachloride and benzene are derived.

The modified σ^{meta} and σ_I values are used to investigate the effect of the β-substituent in β-substituted styrenes on σ_R for *para*-substituents in these systems.

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INTRODUCTION

The Hammett Equation

In 1938 Hammett[1] proposed the relationship

$$\log K^X - \log k^H = \rho\sigma$$

that now bears his name, in an attempt to systematise the effect of substituents on rates and equilibria for reactions of benzenoid compounds. In the above equation K^X is a rate or equilibrium constant for a substituted reactant, K^H is the corresponding constant for the unsubstituted reactant, σ (the substituent constant) is a constant characteristic of the substituent only, and ρ (the reaction constant) is characterist of the reaction under a study and is independent of the substituent.

The substituent constant σ of any substituent X was defined as $\log K^X - \log K^H$ for the ionisation of X-substituted benzoic acids in water at 25^oC. By using σ values for a number of substituents calculated in this way Hammett was able to calculate ρ values for a number of reactions. These ρ values could in turn be used if necessary to calculate σ values for substituents for which acid dissociation constant data in aqueous solution at 25^o were unavailable. Alternativel known σ and ρ values could be used to estimate unknown rate or equilibrium constants for which data were not available.

Unfortunately, various deviations from some of these predictions soon became apparent.[2] These proved invariably to be cases where direct resonance interaction between the substituent and reaction site was possible. In terms of those reactions for which data were available at the time, the phenomenon was, for practical purposes, confined to reactions of

anilines and phenols and their derivatives and involved para-substituents capable of exerting a -R effect. A survey of the data, however, led Hammett to conclude that the extent to which the σ value needed to be modified in each case was approximately independent of the reaction, i.e. the anomalies could be compensated for adequately simply by assigning a second alternative σ value to para -R substituents for use specifically in reactions of anilines and phenols. He referred to these values as σ* constants, although they are now commonly known as σ^- values.

Substituent constants for para - +R substituents for use where the reaction site had -R character did not prove necessary at the time since little data on reactions of this type were available. Subsequently, however, Brown and Okamoto[3] provided a series of "electrophilic" substituent constants", given the symbol σ^+ for use in such situations. These were for the most part based on reactions of Aryl-dimethylcarbinyl chlorides in aqueous acetone. Their real advantage proved to be that they could also be applied satisfactorily to electrophilic aromatic substitution reactions indeed, σ^+ values for some substituents were based on these.

"Normal" substituent constants

Up to the time of Brown and Okamoto the three types of σ constants discussed had proved adequate. However some people were unhappy with the choice of benzoic acid ionisation as the standard reaction in view of the possibility of significant resonance interaction between the carboxyl group (and carboxylate ion) and para- +R substituents. It was felt that a true or "normal" substituent constant should involve

no possibility of resonance interaction at all between the two. Two groups of workers made attempts to eliminate this problem. Van Bekkum, Verkade, and Wepster[4] derived a set of σ constants that they referred to as σ^n values. Their approach was to initially determine a small set of primary σ values for which they considered the Hammett values were reliable. The values chosen were (in addition to H) m-Me, m-F, m-Cl, m-Br, m-I, m-Ac, m-NO_2, and, for reactions involving -R side-chains, p-Ac and p-NO_2. These were used to calculate ρ values for some 80 reactions, and the ρ values were in turn used to calculate σ values for other substituents. These were used as a basis for determining mean σ^n values, the latter being determined by averaging σ values for reactions where resonance interaction between substituent and reaction site was not possible.

At approximately the same time, Taft and co-workers[5] were tackling the same problem, but using a slightly different approach. Their values, which were referred to as σ^o values, were statistically based for all but <u>para</u>- +R substituents. Values for these were derived, not from those reactions which did not involve -R side-chains, but rather from a limited series of reactions in which the reaction site was insulated from the aromatic system by a linkage that could not transmit resonance effects, the -CH_2- group. The two approaches should have led to identical results in theory but this was not borne out in practice. Discrepancies were presumably due to experimental error. Taft's σ^o scale has received the widest degree of acceptance.

Dual Substituent constants or a sliding scale?

With the advent of σ^{o}/σ^{n} values it became apparent that the old system of a $\sigma/\sigma^{+}/\sigma^{-}$ scale needed reconsideration. In theory there was no reason why only a limited number of σ constants for a particular substituent should suffice. In fact, comparison of σ^{o}, σ and σ^{+} values for strong +R substituents showed that the benzoic acid-based σ series really represented an intermediate situation between one of no resonance interaction with the reaction site (σ^{o}) and strong interaction (σ^{+}).

Jaffe[6] had earlier recognised a continuously varying σ scale for electron-donating substituents but held that for electron-withdrawers intermediate values between σ and σ^{-} were not needed. Wepster and co-workers[4], on the other hand felt that their data showed that intermediate values were necessary in both cases for some reactions; and that a multiplicity of values did in fact exist. This implies that in certain circumstances the value of σ can depend on the nature of the reaction site and that a sliding scale is necessary. Currently this is the accepted view, but, in practice intermediate values have not been widely observed.

Various attempts have been made to come to grips with a sliding σ scale. The most common approach is to attempt to resolve σ_{para} values into reaction-dependent and reaction independent contributions. We will consider only three of these in detail, those of Yukawa and Tsuno[7], Ehrenson, Brownlee and Taft[8], and Happer and Wright[9].

The Yukawa - Tsuno Equation

This equation was the first of the three developed and is still widely used, although it has to some extent been

superceded by the second above. In its currently accepted form it expresses the Hammett equation in the form:

$$\log K^X - \log K^H = \rho(\sigma^o + r^+(\sigma^+ - \sigma^o)$$

(an analogous equation for σ^--type reactions was proposed subsequently by Yoshioka and co-workers[10] but this may be considered a relatively trivial extension). Inspection shows that the equation resolves the σ_{para} value into a constant contribution that covers interaction between the substituent and the ring and an additional contribution resulting from direct resonance interaction between the substituent and the reaction site. The major assumption made is that this additional contribution to σ is independent of the nature of the substituent but is instead directly proportional to the difference between the "normal" and "exalted" σ constants. It may be noted that the equation is designed to encompass a range of reaction types varying from σ^o to σ^+/σ^- with r^+/r^- varying from 0 to 1. Subsequently, reactions have been found for which $r > 1$, but this is not really important since the relationship is an empirical one anyway (as are, indeed the others following).

The Dual Substituent Parameter equation of Ehrenson, Brownlee and Taft

This equation, usually referred to as the DSP equation, expresses the Hammett equation in the form

$$\log K^X - \log K^H = \rho_I\sigma_I + \rho_R\sigma_R \qquad \text{----(1)}$$

This represents the resolution of the total electronic effect of the substituent into independent inductive and resonance contributions, and allows the sensitivity of the reaction to each to differ. The parameters ρ_I and ρ_R are seen as measures

of the susceptibility of the reaction site to changes in inductive and resonance effects respectively. They define the particular blend of the two that actually reach the reaction site from the substituent. The symbol $\lambda(= \rho_R/\rho_I)$ is often used to quantify this blend. In the form given above it is very close in concept to the earlier equation of Swain and Lupton[11] which had proved less satisfactory than the Yukawa - Tsuno equation. However in this case the parameters have been derived differently, and, more importantly, the σ_R scale has been extended. The author's recognised that no single σ_R scale could be used to describe the resonance behaviour of substituents in all reaction systems. To circumvent this problem they proposed the use of four discrete scales of σ_R values. These were σ_R^o, $\sigma_{R(BA)}$, σ_R^+ and σ_R^-, corresponding to the resonance contributions present in the σ^o, σ, σ^+, and σ^- scales. Selection of the σ_R scale to be used was based on which of the four fitted the data best, the choice being based on the lowest value of s.d./RMS for the system. The four-scale option gave the DSP equation a considerable advantage over both the Yukawa-Tsuno equation and Swain and Lupton's one.

The Variable Resonance Parameter equation of Happer and Wright

This treatment is closely related to that of Ehrenson, Brownlee and Taft in that it likewise attempts to resolve total electronic effects into inductive and resonance contributions. The difference arises in the approach to the problem of no single σ_R scale being suitable for all reactions. Whereas Ehrenson, Brownlee, and Taft simply proposed a choice of any of four, which must, of course be only an approximation,

Happer and Wright instead proposed a sliding σ_R scale as is indeed likely to be the case. This sliding scale was assumed to be exponentially related to the electron demand placed on the substituent by the reaction site. This means that the σ_R term in the DSP equation is replaced by the much more complex expression:

$$\sigma_R = \sigma_R^{\infty}[1 - (\frac{\sigma_R^{\infty} - \sigma_R^{H}}{\sigma_R^{\infty}})\varepsilon_+]$$

Of the three terms on the right hand side of the equation, σ_R^{∞} and σ_R^{H} were reaction independent properties of the substituent and could be measured and tabulated while the third term, ε_+ (or ε_- for -R substituents) was a reaction dependent variable whose value was substituent independent. Its value increased as the degree of resonance interaction increased, and consequently it was considered to be a measure of the degree of electron demand placed on the substituent by the reaction.

It may be noted that substitution of the above expression for σ_R into (1) increases the number of variables to be correlated from two to three (more accurately from two-and-a-bit to three). While this does not present an insuperable problem, Happer and Wright reduced this back to two by assuming that $\rho_I = \rho_R$ leading to the overall equation

$$\log K^X - \log K^O = \rho(\sigma_I + \sigma_R^{\infty}[1 - (\frac{\sigma_R^{\infty} - \sigma_R^{H}}{\sigma_R^{\infty}})\varepsilon_+])$$

Fitting the equation to the data involved independent determination of ρ using data for meta-substituents followed by determination of the value of ε_+ from tabulations (or graphs) of ε_+ v σ_R for the relevant para-substituents.

A comparison of the two equations shows that the DSP equation is best suited to situations where there is reason to believe that ρ_I and ρ_R may differ significantly and that the latter (the variable resonance parameter equation) is the more appropriate where we would expect $\rho_{meta} = \rho_{para}$ and that none of the four σ_R scales postulated was really suitable. The two scales are not incompatible. The values for ε_+ of 0.45, 0.73, and 2.0 correspond to σ_R^o, $\sigma_{R(BA)}$ and σ_R^+ respectively for +R substituents, and ones of $\varepsilon_- = 0.38$ and $\varepsilon_- = \infty$, $\sigma_{R(BA)}$ and σ_R^- for -R ones. The DSP equation could therefore be considered as four special cases of the VRP equation.

The Application of the Hammett equation and its extensions to NMR chemical shift measurements.

Correlations between substituent parameters and NMR chemical shifts have received much attention and the subject has been recently reviewed in some detail by Ewing[12]. While correlations involving ^1H NMR chemical shifts have been achieved[13] the majority of the work reported in the literature has dealt with ^{19}F and ^{13}C NMR. It is believed that although the traditional Hammett substituent constants characterize electronic differences between initial states and either transition states or products they also are a measure of ground state electronic perturbations caused by substituents and so will be affected by at least some of the factors that influence NMR chemical shifts.

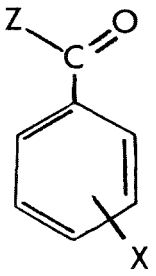
Taft and co-workers[14] found that ^{19}F shielding parameters in *meta*- substituted fluorobenzenes correlated well with σ_I data based on reactivity studies. They considered the correlation to be a sufficiently good one for data of these types to be useful for determining σ_I values for new substituents. They also found that the differences between the ^{19}F shielding parameters for the *meta*- and *para*-substituted derivatives correlated very well with σ_R^o. Since then, Taft has revised his correlations to include a small resonance contribution to the shifts in the meta-series ($\lambda = \rho_R/\rho_I = 0.15$)[15]. Since this early work of Taft's ^{19}F chemical shifts have been used extensively by many groups[16] in attempts to ascertain the relative importance of the π-inductive and direct field mechanisms of transmission of inductive effects.

Early attempts at quantitatively correlating ^{13}C NMR chemical shifts with electronic effects of substituents via substituent constants were hindered by the fact that neat liquids were necessary to get strong enough signals for meaningful spectra to be obtained. The advent of fourier transform techniques brought about great improvements in the precision of measurements made at natural ^{13}C abundance and meant that data could be obtained for samples in dilute solution. Considerable effort has gone into DSP investigations of the shifts of the *para*- ring-carbons of monosubstituted[17] and disubstituted benzenes[18], but it has not proved possible to account for the shifts entirely in terms of inductive and resonance effect. Whether the discrepancies between experiment and theory are due to deficiencies in the equation or to abnormal substituent effects cannot be readily ascertained.

There are clear indications, however, that in these systems substituent chemical shifts are showing different sensitivities to inductive and resonance effects.

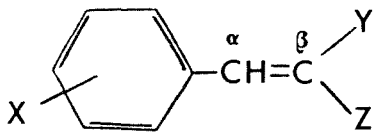
More successful correlations have been obtained for ^{13}C chemical shifts of side-chain carbons, particularly sp and sp^2 ones. Bromilow and Brownlee[19] were able to demonstrate satisfactory correlations of the ^{13}C chemical shifts of the cyano-carbons of both meta- and para-substituted benzonitriles using the DSP equation. Recently Brownlee and coworkers[20] have examined and interpreted the chemical shifts of the carbonyl carbons of a variety of series of compounds of general structure (1).

(1)



The authors concluded as a result of DSP analysis of the data that the direct field effect of the substituent X was a major influence on the substituent induced chemical shift.

The side-chains that have proved the most fruitful in so far as obtaining satisfactory correlations between electronic effects have proved to be ethenyl or substituted ethenyl ones, and in particular those bearing a substituent or substituents on the β-carbon of the ethenyl group (2).



(2)

Data for a considerable number of series have been published, but many are not well suited to precise correlation because they were obtained in concentrated solution or involved insufficient substituents. A list of most of the ones reported to date is given in Table I-1. The effects of substituents on the α-carbon are in general very similar to those observed for the carbonyl carbon in (1). This is, of course expected. It is the resonances for the β-carbons however that are the most important, since there is evidence that electronic effects dominate the substituent chemical shifts* of these to such an extent that other factors can be more or less ignored. It was, in fact, the chemical shifts of these carbons that were used by Happer and Wright[9] as a basis for the calculation of the σ_R^H and σ_R^∞ parameters in their variable resonance parameter equation.

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* The substituent chemical shift (SCS) is the change in chemical shift of a particular resonance that results from the introduction of a substituent into the parent compound.

Table I-1

Literature studies of ^{13}C NMR spectra of Styrene Derivatives*

Y	Z	solvent	reference	comments
H	H	various	21	
H	NO_2	$CDCl_3$, Me_2SO	22	1 M concentration
H	CO_2H	Me_2SO	23	
H	COO^-	H_2O	23	
CN	CN	Me_2SO	23	
Me	Me	CCl_4, $CDCl_3$	23,24	
H	CO_2Et	$CDCl_3$	25	
H	Ph	$CDCl_3$	24	
H	COPh	$CDCl_3$	26,24	1M solution
H	$CO\text{-}Fe^+$	$CDCl_3$	27	
H	$MeSO_2$	$CDCl_3$	28	few meta data
H	CN	$CDCl_3$	29	
Cl	Cl	$CDCl_3$	30	few meta data
Ac	Ac	$CDCl_3$	31	few meta data

* Only substituents for which sufficient meta-data were reported for ρ_{meta} to be determined are listed.

Happer and Wright made two crucial assumptions in their work. The first of these was that the effect of meta-substituents in the ring on the SCS for the β-carbon was directly proportional to σ^{meta} for that substituent, and secondly that the sensitivity of the β-carbon to electronic effects was the same for the meta- and para- positions of the ring, i.e. $\rho^{meta} = \rho^{para}$.

The validity of the first assumption was discussed by Happer in a subsequent paper[21]. He noted that correlations of meta- data for reactions in non-aqueous solvents with meta-C_β SCS data in the same solvent were superior to those obtained using literature σ^{meta} values. The second assumption cannot be justified, but neither can it be refuted. DSP analysis suggests that it is probably correct in at least some cases (e.g. the β,β-dimethylstyrenes, β-nitrostyrenes), and there is no reason to believe that it is not correct for all, since discrepancies can be readily explained as resulting from the use of the fixed point σ_R scales.

The real weakness in the approach used by Happer and Wright lay in their selection of σ_I (and hence σ^{meta}) values. This involved making assumptions as to the effect of solvent on their magnitudes. The data used were obtained in either CCl_4, $CDCl_3$ or Me_2SO solvents and it was very clear that the same σ^{meta} values did not apply in all solvents. In the event the assumption was made that σ_I for the four halogeno substituents was solvent independent over the range of solvents studied. Subsequently Happer took a further look at this assumption[21] and tentatively suggested that σ_I for halogeno substituents might in fact be solvent dependent, and ρ solvent

independent, but evidence in support of this contention was weak.

It was because of the generally unsatisfactory nature of the situation that the work embodied in this thesis was undertaken. It was felt that if an independent method of determining σ_I values in non-aqueous solvents could be developed this could lead to a better understanding of the factors that influence ^{13}C substituent chemical shifts. At the present time it is difficult to decide whether discrepancies in correlations using Happer and Wright's equation, or more especially the DSP equation, are real or whether they simply reflect the use of inappropriate substituent parameters. Ideally, of course, this reassessment of σ_I parameters should be coupled with a reassessment of σ_R ones as well. In practice however, this is more difficult than it appears, because relating values obtained in non-polar solvents to those in water-based ones is hampered by the difficulty of finding series of compounds sufficiently soluble in both. In the end it was decided to simply examine the variation of σ_R with electron-demand in a single solvent, $CDCl_3$, this being the one most widely used in ^{13}C NMR spectrometry. What this really came down to was an examination of the effect of changes in β-substituent or substituents on σ^{para}, since if σ_I is known, σ_R can be determined (provided we assume $\rho^{meta} = \rho^{para}$).

Since the main object of the thesis is to determine the magnitudes of inductive substituent constants, it is appropriate at this point to review previous work in this area.

The Determination of Inductive Substituent Constants

Setting up a scale of σ_I values that are on the same scale as Hammett substituent constants involves two separate tasks. The first of these is developing a system or reaction in which it is possible to measure accurately some property for which the magnitude of substituent induced changes is related in some known way to the magnitude of the inductive effect of the substituent. This usually involves finding a system where the magnitude of the effect is large, which usually implies that the substituent and the "reaction site" are close together, yet steric and resonance effects are absent, or at least independent of the steric effect of the substituent. The second, and perhaps more difficult problem is one of scaling - the conversion of the observed effects, by choice of a suitable proportionality constant, to the Hammett σ scale.

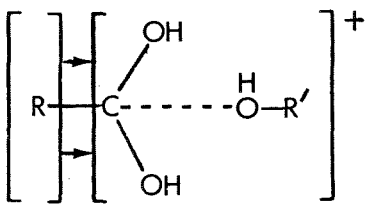
The first serious attempt to establish a quantitative scale of inductive effects was that of Taft.[32] He worked along the lines of proposal made by Ingold in 1930.[33] This involved the comparison of the relative rates of base and acid hydrolysis of esters of α-substituted acetic acids. A series of polar (inductive) substituent constants (σ^* values) were derived using the equation below

$$\sigma^* = \frac{1}{2.48}\left[\log\left(\frac{k}{k_o}\right)_B - \log\left(\frac{k}{k_o}\right)_A\right]$$

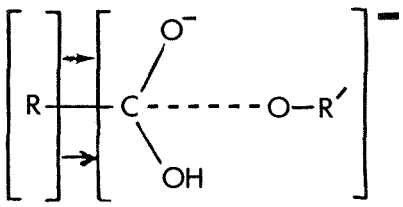
where $\left(\frac{k}{k_o}\right)_B$ is the relative rates of base hydrolysis of the substituted and unsubstituted esters and $\left(\frac{k}{k_o}\right)_A$ is the corresponding expression for the rates of acid hydrolysis.

The factor $\frac{1}{2.48}$ represents an attempt to place σ^* on the same scale as Hammett σ values.

The central argument of this proposal is that the steric and resonance contributions to the transition state energies of the acid and base hydrolyses will in each case be the same and will cancel. The effect of substituent polarity will be much greater in the alkaline case. For the two mechanisms the transition states to be compared are shown below.



Acid
transition state

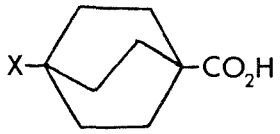


Alkaline
transition state

These proposed transition states differ only by the presence of extra protons in the case of acid hydrolysis. It was argued that the small size of these protons makes them sterically insignificant in interactions with X. It was further argued that resonance interaction with the substituent can only occur in the ground state since both transition states are saturated with respect to possible resonance. Thus the difference in resonance contributions between the ground and transition states, and hence the resonance effect of the substituent will be the same in both the acid and base hydrolyses. Clearly the oppositely charged transition states will react differently to changes in the

polar nature of the substituent.

In an alternative approach Roberts and Moreland[34] prepared a short series of 4-substituted bicyclo-[2.2.2.]-octane-1-carboxylic acids (3)



(3)

and measured their dissociation constants in 50% ethanol. They then proposed an analogous equation to the Hammett equation

$$\log \left(\frac{K^X}{K_H}\right) = \rho'\sigma'$$

for these acids and defined $\rho' \equiv 1.464$ for their dissociation in 50% ethanol at 25°C (the figure of 1.464 was their value for ρ for the dissociation of benzoic acids under the same conditions. This had the effect of bringing their σ' scale into line with Hammett σ values).

Taft[32] later pointed out that his σ^* values correlated very well with Robert's σ' values.

$$\sigma' = 0.45\ \sigma^*$$

and later[35] defined σ_I as

$$\sigma_I = \sigma' = 0.45\ \sigma^*$$

Although Roberts and Moreland prepared only a short series of acids other workers[36-39] have added to these. In addition further σ_I values based on other aliphatic reactivity data, particularly the dissociation constants of acetic acids, have become available.

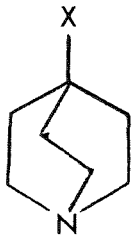
As has been noted previously, Taft and co-workers[14] also found that there was a good correlation obtained between σ_I and the ^{19}F NMR chemical shifts of meta-substituted fluorobenzenes. Data for these compounds in a variety of solvents was used to investigate the solvent dependence of σ_I. Earlier Ritchie and Lewis[36] had investigated the solvent dependence of σ' and found this to be significant. Taft found that solvent dependences observed in their investigation could be accounted for by specific chemical interactions between solvent and substituent. For example, those substituents having measurable base strengths showed shifts to lower field in trifluoroacetic acid and those substituents capable of hydrogen bonding showed similar shifts in protonic solvents. Other effects suggested to be operating were solvent polarity effects on the amide and ester substituents, and specific interactions of solvents capable of addition to poorly resonance-stabilised carbonyl groups such as -CHO, $-COCF_3$ or -COCN.

Taft did, however, in this study note a group of substituents whose inductive effects appeared to be solvent independent. These were -Me, -Ph, H, Br, CF_3, F, OCF_3 and SF_5, but the average shielding parameters for these substituents do not give a satisfactory correlation with the σ_I parameters currently proposed by Ehrenson, Brownlee and Taft.[8] It was noted earlier in this introduction, however, that Taft now recognises a small contribution from resonance to these shielding parameters.

Charton[40] assumed that steric effects were negligible in substituted acetic acid ionisations. On this assumption he derived a σ_I scale based on the dissociation constants of acetic acids and scaled using Roberts and Moreland's data. This method is best suited to small substituents that do not interfere with solvation of the carboxylate ion.

One of the major deficiencies of using the 4-X-bicyclo-[2.2.2.]octane-1-carboxylic acid series (3) as a standard (apar from the synthetic difficulties involved) is the relative insensitivity of the reactions to inductive effects, which increases the significance of measurement errors. One solution to this problem is to bring the reaction site a little nearer the substituent.

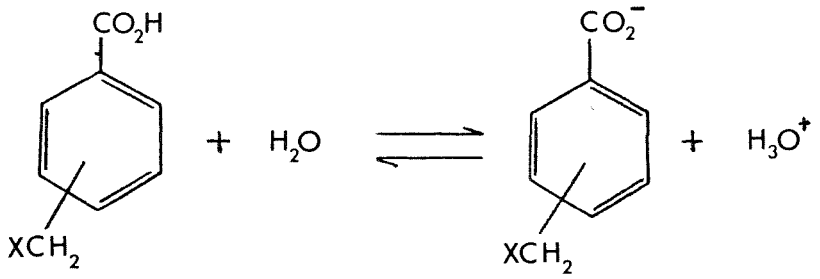
Grob and Zergenji[41] looked at the 3-substituted quinuclidines as a possible alternative series but felt that the possibility of free rotation in the case of unsymmetrical substituents such as -OMe could lead to varying substituent dipole orientation and hence an inaccurate polar field contribution to σ_I. Grob and Schlageter[42] then studied the 4-substituted quinuclidines (4).



(4)

They were able to show a good correlation between the pKa's of the quinuclidinium ions in water and σ_I. They claimed that this system had the advantages of constant orientation of substituent dipoles, absence of steric effects and that quinuclidines showed a much greater response to polar substituent effects than the bicyclo[2.2.2.]octane carboxylic acids. They also were able to show a significant solvent dependence for at least the cyano substituent.

In an alternative approach Exner and Jonas[43] studied benzoic acid ionisations but attempted to eliminate resonance effects by interposing a methylene group between the substituent and the ring.



While the increased distance between X and the reaction site decreased the sensitivity of the reaction to substituent effects they were still able to obtain good correlations with literature σ_I values. They further noted that the ρ_I^{para} appeared to be slightly greater than ρ_I^{meta} ($\rho^{para}/\rho^{meta} = 1.14$).

Some years later, Fischer, King, and Robinson[44] prepared an extensive series of 2-, 3-, and 4-XCH_2-substituted

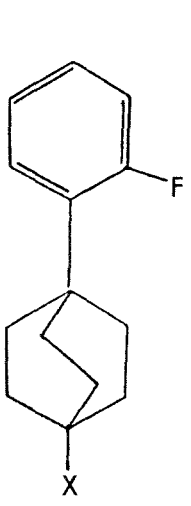
pyridines and measured the pKa's of their conjugate acids in H_2O at 25^o. These systems were much more sensitive to the inductive effect of substituents since the distance between the substituent and the reaction site is two atoms fewer. They found that their data correlated very well with currently accepted σ_I constants. They derived σ_I values for some new substituents and proposed a revised σ_I scale. Their data, in contrast to that of Exner and Jonas[43] indicated that the inductive effect operated equally effectively from the meta and para positions.

Until relatively recently the only serious attempt to use NMR chemical shift data as a source of σ_I constants was that mentioned earlier of Taft and co-workers.[14] All of the other studies, it will be noted, are based on reactivity studies, where it is clear that what is being measured is a property in which the inductive effect of the substituent can be assumed to be the only significant factor influencing the change in reactivity observed. In attempting to use physical data such as NMR chemical shifts, there is an initial problem in establishing the absence or at least insignificance of factors other than inductive effects that can contribute to the observed substituent-induced changes. If this difficulty can be overcome, however, then it is possible to obtain accurate data under a relatively wide range of conditions very quickly. Solving the first problem though is not easy. The results of some attempts to interpret NMR data in terms of inductive and resonance effects are surveyed in two reviews.[12,13] These were not encouraging.

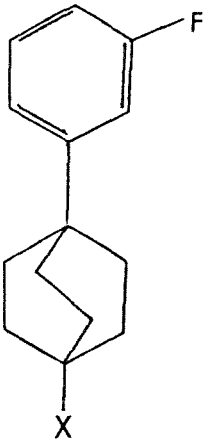
So far as studies of inductive effect - dominated systems are concerned, they have been few in number. Shapiro[45] examined the ^{13}C NMR chemical shifts of α-substitutud toluenes. For the para-ring carbon DSP analysis suggested that inductive effects were an important influence on SCS, but when the degree of precision of the data is taken into account it becomes obvious that other effects are operating as well. In general DSP analysis of para-ring carbons in benzene series have shown that resonance effects have a much greater influence than inductive effects, and it is possible that in the α-substituted toluenes resonance effects have not been eliminated entirely.

Bradamante and Pagani[46] looked at the same series and also at the ^{19}F shifts in α-substituted para-fluorotoluenes among other compounds of similar type. They derived a σ_I scale that agreed with accepted σ_I values for many substituents but there were some exceptions.

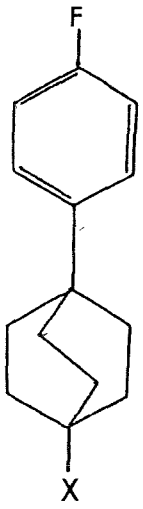
Adcock and Khor[16b,16h] decided to avoid the potential problems inherent in interposing a $-CH_2-$ linkage between X and the aromatic ring by using a bicyclo[2.2.2.]octylene one instead. This unfortunately decreases the sensitivity of the shifts to substituent effects. They obtained ^{19}F data for the ortho-, meta- and para- fluorobenzenes and ^{13}C NMR for the benzenes themselves.



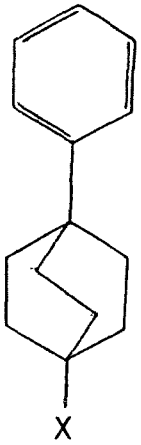
(5)



(6)



(7)



(8)

The ^{19}F data were obtained in five different solvents, (DMF, methanol, benzene, methylene chloride and cyclohexane, and the ^{13}C NMR data in two (deuterochloroform and cyclohexane). Very good correlations with σ_I were observed for the ^{19}F shifts for (6) and (7) and for the ^{13}C shifts of the <u>para</u>-ring carbons in (8). Unfortunately, because of the high degree of attenuation of the substituent effects measurement errors can be quite significant. This is especially true for the case of the ^{13}C measurements.

This survey of the σ_I values and their measurement has been representative rather than comprehensive. The most widely accepted values at the present time are those of Ehrenson, Brownlee and Taft.[8] The basis on which these were selected is unclear, but they would seem to be predominantly statistically based. Recently Charton[47] has reviewed the situation to date and compiled a series, also statistically based, but

incorporating more recent data. For the majority of substituents agreement between the two is excellent, but Charton's is the more comprehensive of the two. In general his tabulation will be used in this work except in the case of DSP analysis of data, where Ehrenson, Brownlee, and Taft's set should be more appropriate.

In seeking to obtain a compilation of values more suitable for use in non-protic solvents it was felt that the best method was to seek a system or systems where good σ_I correlations could be expected and accurate data could be quickly and easily obtained. ^{13}C NMR studies of the α- and β-carbons of styrene derivatives seemed the best possibility, but there was the problem of eliminating resonance effects as far as possible without attenuating inductive effects too much. It was felt that the approach used by Exner[43] and by Fisher[44] i.e. the use of XCH_2- substituents might prove a fruitful one, and this was chosen. The XCH_2-substituted styrenes had the advantage of, in nearly all cases, being known compounds but this was outweighed by the disadvantages of the experimental difficulties of preparing and handling small quantities of readily polymerisable liquids. Instead the XCH_2-substituted methyl cinnamates were chosen. While most of these were unknown and there was the additional problem introduced by the use of a polar β-substituent capable of interacting with the solvent, the advantages tended to outweigh these disadvantages. They were easily prepared; mostly crystalline solids, and stable. In addition the resonances of the α-

and β-carbons were sufficiently separated from those of the aromatic carbons for these to be easily identified.

^{13}C NMR spectra of these were obtained in six solvents ethanol, dimethyl sulphoxide, acetone, deutero-chloroform; carbon tetrachloride and benzene. Ethanol was the most water-like solvent in which the compounds could be dissolved and it was assumed that literature σ_I values might apply in this case. In the event it was found that this was not entirely true.

In addition to the series of meta- and para-XCH_2-substituted methyl cinnamates a series of similarly substituted fluorobenzenes was prepared and their ^{19}F chemical shifts determined. The main aim of this was to, if possible, provide support for σ_I values obtained from the ^{13}C work.

Thus σ_I values obtained were then used to resolve the Hammett σ constants obtained in our ^{13}C NMR study of the β-carbons of a number of series of β-substituted styrenes, in order to investigate the effect of varying the β-substitute on σ_R for para-substituents.

EXPERIMENTAL

All solvents used were technical grade. The petroleum ether (50-70^{o} fraction) was subsequently distilled from phosphorous pentoxide. Diethyl ether (hereafter referred to as 'ether') was purified by distillation from sodium hydride. Dimethyl sulphoxide was dried by refluxing for three hours over sodium hydroxide followed by distillation from fresh sodium hydroxide. Unless otherwise stated, all other solvents were used without further purification.

Most commercially available reagents were used without further purification as were compounds which had been prepared within the department for earlier studies.

Laporte type H 100-200 mesh alumina, grade B.S.S. Sorbsil silica gel and 100-200 mesh Florisil were used as required for column chromatography. Thin layer chromatography was carried out on TLC grade alumina and silica gel, eluted with ether/petroleum ether mixtures and visualised by spraying with a 10% w/w solution of phosphomolybdic acid in ethanol. High performance liquid chromatography was performed using a Varian model 5000 liquid chromatagraph in conjunction with a Varian UV-50 variable wavelength detector, using mixtures of hexane and dichloromethane as solvent and a Zorbax CN type column.

Proton NMR spectra were recorded on either a Varian T-60 or a Varian EM360 60 MHz NMR spectrometer and were recorded for samples dissolved in either spectroscopy grade carbon tetrachloride or deuterochloroform with tetramethylsilane as an internal standard.

Carbon -13 NMR spectra were obtained on a Varian CFT-20 NMR spectrometer operating at 80 MHz and with a probe temperature of 33° C. All spectra, with the exception of those of the substituted methyl cinnamates, were determined for solutions of 0.4 M in deuterochloroform with tetramethylsilane as an internal standard. Spectra of the methyl cinnamates were determined for solutions of 0.2 M or less in spectroscopy grade acetone, dimethyl sulphoxide, ethanol, deuterochloroform, carbon tetrachloride and benzene. For each solvent spectra were referenced to tetramethylsilane as an internal standard. Spectra for the β-bromostyrenes and cinnamonitriles were generally recorded for mixtures of the cis- and trans-isomers.

Fluorine-19 NMR spectra were recorded on a Varian FT-80A NMR spectrometer, operating at 74.838 Hz, with a probe temperature of 30° C. Spectra were determined for solutions of 0.2 M or less in acetone, dimethyl sulphoxide, chloroform, carbon tetrachloride and benzene and were referenced externally to trifluoroacetic acid.

High resolution mass spectra were recorded on an A.E.I. MS902 mass spectrometer operated at a resolving power of 10,000.

All melting points are uncorrected.

Microanalyses were carried out at the University of Otago.

PREPARATION OF PRECURSORS

Mono-Substituted Benzaldehydes

Table E-1 The Mono-Substituted Benzaldehydes used as Precursors.

Substituent	Source
H	Riedel-De Haën, Reagent grade
3-CH_3	Prepared by a Sommelet reaction on 3-methyl-benzyl bromide
3-CH_2CH_3	Prepared by reaction of the phenylmagnesium bromide with triethyl orthoformate
3-OCH_3	L. Light and Co. Ltd., reagent grade
3-OC_6H_5	Fluka, reagent grade
3-F	Sommelet reaction on 3-fluorobenzylamine
3-Cl	BDH laboratory reagent
3-Br	Riedel-De Haën
3-I	Sommelet reaction on 3-iodobenzyl bromide
3-CF_3	Reaction of the phenylmagnesium bromide with triethyl orthoformate or N,N-dimethylformamide
3-CN	Sommelet reaction on 3-cyanobenzyl bromide
3-NO_2	Koch-Light Laboratories, reagent grade
4-CH_3	Koch-Light Laboratories, reagent grade
4-CH_2CH_3	Formylation of ethylbenzene
4-OCH_3	BDH Laboratory reagent
4-$N(CH_3)_2$	Unilab Laboratory reagent
4-F	Koch-light Laboratories, reagent grade
4-Cl	Fluka, reagent grade
4-Br	Koch-light Laboratories, reagent grade
4-I	Sommelet reaction on 4-iodobenzyl bromide
4-CN	Available from within the department
4-NO_2	Fluka, reagent grade

Of the twenty-one substituted benzaldehydes required as precursors and listed in Table E-1, thirteen were available as commercial preparations and were used without further purification. Of the others 4-cyanobenzaldehyde was available from within the department, it having been prepared for previous studies. Five remaining aldehydes were prepared by a Sommelet[48] reaction on the corresponding substituted benzylamine or benzyl bromide. 3-Trifluoromethylbenzaldehyde and 3-ethylbenzaldehyde were prepared by the reaction of the appropriate phenylmagnesium bromide with a formic acid derivative.[49] 4-Ethylbenzaldehyde was prepared by the direct formylation of ethylbenzene[50]

3-Methylbenzaldehyde

In order to prepare 3-methylbenzaldehyde, 3-methylbenzyl bromide was obtained by a Wohl-Ziegler bromination of meta-xylene.[51]

(i) 3-Methylbenzyl bromide:- Meta-Xylene (61 g), N-bromosuccinimide (70 g) and dibenzoyl peroxide (1 g) were refluxed in 300 mL carbon tetrachloride for 1 h. The reaction mixture was allowed to cool and then filtered under suction. The solvent was removed from the filtrate by distillation under reduced pressure, leaving 86 g of a pale yellow oil.

The crude product was carefully distilled under reduced pressure, with 3-methylbenzyl bromide comprising the fraction boiling in the range 50-65^{o}C/2 mm. The yield was 56.5 g (78%, based on N-bromosuccinimide) and the product was used without further purification in the preparation

of 3-methylbenzaldehyde.

(ii) 3-Methylbenzaldehyde:- 3-Methylbenzyl bromide (56.5 g) and hexamine (80 g) were refluxed in 100 mL of 50% aqueous acetic acid for 75 minutes. The mixture was cooled and extracted with ether. The ether solution was washed with water, then with a saturated solution of sodium bicarbonate, and finally with water again. It was dried over anhydrous magnesium sulphate and the ether removed by distillation under reduced pressure. 3-Methylbenzaldehyde (33.8 g; 92%, based on 3-methylbenzyl bromide) was obtained as a pale yellow oil and was used in subsequent preparations without further purification.

3-Fluorobenzaldehyde

3-Fluorobenzylamine (3 g, reagent grade from L. Light and Co. Ltd.) and hexamine (4.5 g) were refluxed in 15 mL of 50% aqueous acetic acid for 2 h. The cooled reaction mixture was extracted with ether. The combined extracts were washed with water, saturated sodium bicarbonate solution, and water again then dried over anhydrous magnesium sulphate. Finally the ether was evaporated to yield 2.6 g (87% , based on 3-fluorobenzylamine) of the crude aldehyde as a pale yellow oil. This was used without further purification in the subsequent condensation reactions.

3-Iodobenzaldehyde

3-Iodotoluene was prepared from 3-toluidine via the Sandmeyer reaction[52]. 3-Iodobenzaldehyde was prepared by a Sommelet[48] reaction on 3-iodobenzyl bromide produced by the bromination of this 3-iodotoluene.

(i) 3-Iodotoluene:- 3-Toluidine (27 g) was dissolved in 60 mL of concentrated hydrochloric acid and 60 mL of water and the solution was stirred vigorously and cooled to below 10^{o} C. A solution of 18.5 g sodium nitrite in 40 mL water was added at such a rate that the temperature of the reaction solution remained below 10^{o} C. After the addition of the nitrite was complete a solution of 44 g potassium iodide in 50 mL water was added slowly with vigorous stirring. The reaction mixture was then stirred at room temperature for 1 h and then warmed on a steam bath for 15 minutes. Sodium metabisulphite (2 g) was stirred into the cooled mixture to destroy any iodine present. The solution was made alkaline with a 10% sodium hydroxide solution and steam distilled. Extraction of the distillate with ether followed by drying over anhydrous magnesium sulphate and removing the solvent by distillation under reduced pressure yielded 48 g (87%, based on 3-toluidine) of crude 3-iodotoluene. This was used to prepare 3-iodobenzyl bromide without further purification.

(ii) 3-Iodobenzyl bromide:- 3-Iodotoluene (16.8 g), N-bromosuccinimide (17 g) and dibenzoyl peroxide (1.5 g) were refluxed in 100 mL of carbon tetrachloride for 1 h. The solution was cooled and filtered. The filtrate was washed with a 0.5 M solution of sodium thiosulphate and then with water. The carbon tetrachloride solution was dried and evaporated to yield a dark red oil. Proton NMR showed this to be only about 30% 3-iodobenzyl bromide. However this mixture was used without further purification to prepare 3-iodobenzaldehyde.

(iii) 3-Iodobenzaldehyde:- Hexamine (3.6 g) was added to the impure 3-iodobenzyl bromide prepared above and the mixture was refluxed with stirring in 50 mL of chloroform for 2½ h. The hexaminium salt produced was filtered from the cooled solution, washed twice with chloroform and air dried. It was then refluxed in 50 mL of 50% aqueous acetic acid for 2 h. The cooled solution was extracted with ether and the combined extracts washed with water, saturated sodium bicarbonate solution, and water again. The ether solution was dried over anhydrous magnesium sulphate and evaporated to yield 3.4 g (19%, based on 3-iodotoluene) of 3-iodobenzaldehyde, with the majority of the loss being in the bromination step.

3-Trifluoromethylbenzaldehyde

3-Trifluoromethylbenzaldehyde was prepared by two similar methods. Both involved the reaction of 3-trifluoromethylphenylmagnesium bromide with a formic acid derivative,[49] namely triethyl orthoformate in one case and N,N-dimethyl formamide in the other.

Method (i):- Magnesium turnings (2 g) were dried by heating in a flask over a flame whilst flushing with dry nitrogen. The flask and magnesium were then allowed to cool under an atmosphere of dry nitrogen and 20 mL dry ether was poured over the cooled magnesium turnings. (The ether had been dried by distillation from sodium hydride, then by distillation from lithium aluminium hydride and stored over sodium wire). 3-Bromobenzotrifluoride (5 g; Sigma reagent grade, dried by standing over calcium chloride) was added

and the reaction started almost immediately. A further 11.8 g 3-bromobenzotrifluoride in 30 mL of dry ether was added at such a rate as to keep the solvent just refluxing with the heat of the reaction. After the addition of all the halide (30 minutes) the solution was refluxed under an atmosphere of dry nitrogen for a further two hours. Triethyl orthoformate (13.5 g in 30 mL of dry ether) was carefully added and the solution refluxed for another 5 h.

At the end of this time most of the ether was distilled off and the dark brown residue allowed to stand overnight. Crushed ice (30 g) and 75 mL of 0.5 M hydrochloric acid were then added and the mixture refluxed for 30 minutes. It was then allowed to cool and extracted with ether. The combined extracts were washed with water and dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure leaving 10.5 g of a dark orange oil. Proton NMR indicated that the product was about 50% aldehyde. The approximate yield by this method was therefore 40% (based on 3-bromobenzotrifluoride).

Method (ii):- 3-Trifluoromethylphenylmagnesium bromide was prepared from 5 g 3-bromobenzotrifluoride and 0.55 g magnesium turnings in a similar manner as was described in method (i) above. N,N-dimethylformamide (2 g, dried by stirring over potassium hydroxide over night then distillation from calcium oxide) in 10 mL dry ether was added and the solution refluxed for a further 2 h. It was then poured into a mixture of 100 mL saturated ammonium

chloride solution and 100 g crushed ice. This aqueous mixture was extracted with ether and the extracts washed with water, dried over anhydrous magnesium sulphate, and the solvent removed under reduced pressure to leave 3.5 g of an orange oil. Proton NMR showed this to be about 60% aldehyde giving a yield, based on 3-bromobenzotrifluoride, of 54%, which is marginally better than that by method (i).

The impurities resulting from both methods are likely to be α,α,α-trifluorotoluene and unreacted 3-bromobenzotrifluoride. The aldehyde produced was used in subsequent reactions without further purification.

3-Cyanobenzaldehyde

3-Cyanobenzaldehyde (2.5 g) was prepared from 3-cyanobenzyl bromide (5 g, Aldrich reagent grade) by a Sommelet reaction in the same way that 3-methylbenzaldehyde was prepared from 3-methylbenzyl bromide.[48] The yield, based on 3-cyanobenzyl bromide was 76%.
The white crystalline aldehyde was used subsequently without further purification.

3-Ethylbenzaldehyde

3-Bromoethylbenzene, prepared by a Wolff-Kishner reduction[53] of 3-bromoacetophenone, was used to prepare 3-ethylphenylmagnesium bromide, which was reacted with triethyl orthoformate to give 3-ethylbenzaldehyde.

(i) 3-Bromoacetophenone[54]:- Redistilled acetophenone (40 g) was added slowly with stirring to 113 g aluminium chloride in a one-litre three-necked flask fitted with a

reflux condenser, a "Tru-Bore" stirrer and a dropping funnel. The addition took 45 minutes. Bromine (64 g) was then added dropwise to the stirred mixture over a period of 20 minutes. The mixture was stirred for a further 1 h after which time it solidified. The solid mass was allowed to stand for 30 minutes, then melted by warming on a steam bath and poured onto a mixture of 100 g ice and 100 mL of concentrated hydrochloric acid. The aqueous mixture was extracted with ether and the combined extracts washed with water, saturated sodium bicarbonate solution and finally with water again. The ether solution was dried over anhydrous magnesium sulphate and the solvent removed under reduced pressure to leave 64 g of dark oil. This crude product was distilled under vacuum to give 48 g (72%, based on acetophenone) 3-bromoacetophenone with bp 78-82^{o}C /2 mm.

(ii) 3-Bromoethylbenzene:- Potassium hydroxide (8.4 g) was dissolved in 20 mL diethylene glycol. 10 mL hydrazine hydrate (99-100%) was added to the stirred solution followed by the addition of 10 g 3-bromoacetophenone. The mixture was refluxed with stirring for 1 h and then steam distilled. Extraction of the distillate with ether followed by drying and evaporating the ether solution yielded 6.6 g (71%, based on 3-bromoacetophenone) of 3-bromoethylbenzene, a colourless oil.

(iii) 3-Ethylbenzaldehyde:- 3-Ethylphenylmagnesium bromide was prepared from 6.6 g 3-bromoethylbenzene and 0.95 g magnesium turnings in a similar way to that described for the preparation of 3-trifluoromethylphenylmagnesium bromide

earlier. Triethyl orthoformate (6.5 g) in 15 mL dry ether was added to the grignard solution which was then refluxed for 5 h. The work-up procedure was the same as that previously described and 4.5 g dark orange oil resulted.

The crude product was distilled under vacuum to yield 1.9 g (40%, based on 3-bromoethylbenzene) of 3-ethylbenzaldehyde in a fraction boiling at 70-80°C /2 mm.

4-Iodobenzaldehyde

4-Iodobenzyl bromide, prepared by a sidechain bromination[51] of 4-iodotoluene, was converted to 4-iodobenzaldehyde by a Sommelet reaction.[48]

(i) 4-Iodobenzyl Bromide:- Reaction of 4-iodotoluene (17, g, BDH laboratory reagent) with N-bromosuccinimide (17 g) and dibenzoyl peroxide (1.5 g) under the conditions used for the 3-iodotoluene yielded 24 g of crude 4-iodobenzyl bromide. Proton NMR indicated that the product was about 75% pure.

(ii) 4-Iodobenzaldehyde:- The crude 4-iodobenzyl bromide was converted to the aldehyde, once again by the same method used for the meta-isomer. The yield of 4-iodobenzaldehyde was 7.6 g (43%, based on 4-iodotoluene) of cream crystals and the product was used in subsequent reactions without further purification.

4-Ethylbenzaldehyde[50]

Ethylbenzene (3 g) in 20 mL dichloromethane was cooled with stirring in an ice-water bath. Titanium tetrachloride (9 g) was then added dropwise to the

stirred,cooled solution. The addition took 5 minutes after which time 2.7 g dichloromethyl methyl ether in 15 mL dichloromethane was added over a further period of 20 minutes. Cooling and stirring was maintained throughout, and for a further 10 minutes. The reaction mixture was then allowed to rise to room temperature and was stirred for 20 minutes and finally was stirred at reflux for a further 20 minutes.

The dichloromethane solution was poured into a separating funnel containing 100 g ice and the mixture shaken. The organic layer was collected and the aqueous layer extracted with two additional portions of dichloromethane. The combined extracts and original organic layer were washed with water, dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure. This yielded 3 g (79%, based on ethylbenzene) of crude 4-ethylbenzaldehyde which was used in subsequent preparations without further purification.

Cinnamic Acids

An extensive series of mono-substituted cinnamic acids was required as a precursor to the preparation of the β-bromostyrenes and methyl cinnamates. Five of the required acids had been prepared within the department for previous studies. The remaining eighteen were all prepared by Knoevenagel[55] condensations of the appropriate benzaldehyde with malonic acid. As the same experimental

method is applicable to all the acids prepared, only a general procedure will be outlined here.

Preparation of a Cinnamic Acid

The benzaldehyde (0.1 mole), malonic acid (0.12 mole) and 10 mL pyridine were stirred at 100° C for 3 h. After this time 250 mL water was added along with enough sodium carbonate to dissolve any precipitated acid. The solution was boiled with decolourising charcoal for 5 minutes then filtered and the filtrate chilled in an ice-bath. Excess concentrated hydrochloric acid was carefully added to the stirred and cooled solution. The precipitated cinnamic acid was filtered by suction, washed several times with water and air dried.

All the cinnamic acids prepared were white or off-white powders and were all used without any attempt at further purification except in those cases where the aldehyde substrate was known to be impure. In these cases the product was merely washed with chloroform which rid the sample of any less polar residues.

Table E-2 contains a summary of the preparations of all the cinnamic acids used as precursors in this study. The yields quoted are based on the mono-substituted benzaldehydes.

Table E-2 Summary of the Preparations of the Cinnamic Acids

Substituent	Wt. Aldehyde Used (g)	Wt. Malonic Acid Used (g)	Yield
3-CH_3	10.0	10.0	10.9 g (81%)
3-OCH_3	6.5	5.7	7.0 g (83%)
3-OC_6H_5	1.0	0.7	0.9 g (72%)
3-C_2H_5	1.3	1.3	0.8 g* (44%)
3-NH_2	Available from within the department		
3-F	1.0	1.0	0.5 g (40%)
3-Cl	7.7	5.7	8.9 g (89%)
3-Br	2.0	1.4	1.7 g (69%)
3-I	1.0	0.6	0.8 g (67%)
3-CF_3	2.0	1.5	1.1 g* (46%)
3-CN	1.3	1.1	1.1 g (64%)
3-NO_2	Available from within the department		
4-CH_3	25.2	18.0	22.7 g (67%)
4-OCH_3	Available from within the department		
4-OC_6H_5	Available from within the department		
4-C_2H_5	4.0	3.6	0.42 g* (8%)
4-$N(CH_3)_2$	Available from within the department		
4-F	1.0	1.0	1.0 g (77%)
4-Cl	7.7	5.7	7.1 g (71%)
4-Br	3.0	1.9	1.6 g (45%)
4-I	1.0	0.6	0.8 g (68%)
4-CN	4.0	4.0	3.5 g (67%)
4-NO_2	4.3	3.0	3.0 g (54%)

* Impure starting material resulted in a low yield of product which required further purification.

β-Bromostyrenes

With the exception of 4-dimethylamino-β-bromostyrene, all members of this series were prepared from the corresponding cinnamic acid dibromides. The cinnamic acid dibromides were made by the reaction of the cinnamic acids with molecular bromine in acetic acid solution. The following paragraph outlines the general experimental procedure and Table E-3 summarises the individual preparations for the cinnamic acid dibromide series. All yields quoted are based on the cinnamic acids and the dibromides prepared were all used without further purification.

Preparation of a Cinnamic Acid Dibromide

The cinnamic acid (0.05 mole) was stirred in glacial acetic acid (20 mL) and maintained at 100° C in a boiling water bath. Bromine (0.05 mole) in glacial acetic acid (50 mL) was added dropwise over the period of 1 h. The heating and stirring was continued for a further 2 h after the addition was complete, and then the solvent was removed by distillation under reduced pressure. The orange solid residue was washed with water and air dried, to leave the cinnamic acid dibromide as a white or cream powder.

Preparation of the β-bromostyrenes

The β-bromostyrenes were made from the cinnamic acid dibromides by the method of Grovenstein and Lee[56]. This is in fact two very similar methods for the partially selective preparation of the cis- and trans-isomers. Method A, outlined below, was used to prepare the trans-β-bromostyrenes. Often however, a significant quantity of the cis-isomer was also produced by this method. This

Table E-3 Preparations of Cinnamic Acid Dibromides from Cinnamic Acids

Substituent	Wt. Cinnamic Acid Used (g)	Wt. Bromine Used (g)	Yield
H	5.3	5.70	10.1 g (91%)
3-Me	6.0	6.0	11.5 g (96%)
3-OMe	5.0	5.0	8.0 g (84%)
3-F	0.7	0.7	1.2 g (89%)
3-Cl	5.6	5.0	8.1 g (77%)
3-Br	1.7	1.9	2.0 g (69%)
3-CF_3	1.1	1.7	1.5 g (77%)
3-CN	1.0	1.9	1.5 g (78%
3-NO_2	3.0	2.6	4.1 g (76%)
4-Me	5.0	5.0	4.1 g (42%)
4-OMe	Available from within the department		
4-F	2.0	1.9	2.9 g (74%)
4-Cl	5.6	5.0	9.1 g (86%)
4-Br	1.0	0.8	1.2 g (73%)
4-CN	3.5	3.3	4.6 g (69%)
4-NO_2	3.0	2.5	4.1 g (75%)

occurred to the greatest extent with the electron withdrawing substituents and in fact, in the preparation of 4-nitro-β-bromostyrene by method A only the cis-isomer was produced.

Method B tended to produce a higher proportion of the cis-isomer and was used when the ^{13}C NMR spectrum of the product from method A did not clearly show the presence of the cis-β-bromostyrene.

Trans-β-bromostyrene could also be prepared from the cis-isomer by a photo-isomerisation. The experimental procedure for this is described under the heading "method C".

Method A

The cinnamic acid dibromide (0.01 mole) was stirred in 25 mL water. Sodium hydroxide solution (1M) was added until the solution was just neutral toward phenolphthalein. With continued stirring the solution was warmed to 78°C and maintained at that temperature for 45 minutes. During this time sufficient sodium hydroxide solution was added to maintain the neutrality of the reaction mixture. After cooling, the solution was extracted with carbon tetrachloride. The combined organic extracts were washed with a saturated solution of sodium bicarbonate, a 0.5 M solution of sodium thiosulphate, and water, then dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to leave the β-bromostyrene generally as an oil or a low melting solid. Any impurities were usually removed by a filtration column on alumina or by recrystallization from ethanol/water mixtures.

Method B

The cinnamic acid dibromide (0.01 mole) was dissolved in 20 mL absolute ethanol and sodium ethoxide/ethanol solution (1 M) was added to make the reaction mixture just neutral to phenolphthalein. The ethanol solution was then heated to reflux and refluxed for 45 minutes more. During this time sufficient sodium ethoxide/ethanol solution was added to maintain the neutrality. The reaction solution was then concentrated to half its volume and rediluted with water. The aqueous solution was extracted with carbon tetrachloride and the combined organic extracts washed, dried, and evaporated in the same way as described in method A. The cis-β-bromostyrenes so produced were generally oils and were not further purified for the purpose of obtaining a ^{13}C NMR spectrum.

Method C

A sample of the cis-β-bromostyrene was dissolved in benzene in a quartz flask with reflux condenser attached and irradiated with U.V. light from a commercial "sun lamp" for 3-6 h. The solvent was removed by distillation under reduced pressure to leave the trans-β-bromostyrene. No further purification was necessary for the purpose of obtaining a ^{13}C NMR spectrum. Apart from the cis to trans isomerisation the sample was generally unaffected by the UV light and yields were close to 100%.

None of the β-bromostyrenes prepared was obtained as one absolutely pure geometric isomer. Most members

of this series are well documented in the literature but for those compounds which were new, satisfactory elemental analyses were obtained for the cis/trans mixtures.

Table E-4 contains a summary of the preparations, cis:trans ratios and physical appearances of the β-bromostyrenes prepared for this study. The yields are given as percentages based on the cinnamic acid dibromide. The special preparation of 4-dimethylamino-β-bromostyrene is described below.

Para-dimethylamino-β-bromostyrene

This compound was known to be unstable towards heat and light so the method of Barbieri[57] was employed for its preparation. Para-dimethylaminocinnamic acid (1-2 g) was dissolved in 10 mL chloroform and the flask cooled in an ice/salt bath. Bromine (5 g) in 8 mL chloroform was added dropwise with stirring at such a rate that the temperature of the reaction solution is kept between -5 and 0^{o} C. After the addition, the solution was stirred for a further 45 minutes at -3^{o} C. It was then transferred to a separating funnel and washed with a cold sodium sulphite solution (0.5 M), with a cold sodium carbonate solution (0.2 M) and finally with water. The chloroform solution was dried over anhydrous sodium carbonate and the solvent removed by distillation under reduced pressure without heating. This yielded 0.35 g (25%, based on the cinnamic acid) of the β-bromostyrene as orange crystals m.p. 119-122^{o} C (lit.[57] 123-124^{o} C). The product was stored refrigerated and in the dark.

Table E-4 Preparations of β-Bromostyrenes

Ring substituent	Method*	Yield (%)	cis:trans	m.p. (expt)	m.p. (lit.)	Ref.
H	A	52	1 : 4	oil		
3-CH_3	A	59	1 : 4	oil		
"	B	66	5 : 1	oil		
3-OCH_3	A	24	1 : 4	oil		
3-F	A	41	2 : 1	oil		†
3-Cl	A	35	2 : 1	oil		†
3-Br	A	42	1 : 3	oil		†
3-CF_3	B	41	~100% cis	oil		
"	C		~100% trans	oil		
3-CN	B	43	~100% cis	31-4°		†
"	C		<1 : 8	75-6°		†
3-NO_2	A	15	8 : 1	oil	7.5-8.5°	58
4-CH_3	A	72	1 : 3	42-3°	40°	59
	B	68	3 : 1	oil		†
4-OCH_3	A	64	1 : 7	46-8	55°	60
4-$N(CH_3)_2$	see text	25	~100% trans	119-20°	123-4°	57
4-F	A	67	<1 : 4	41-2°		†
"	B	65	~100% cis	oil		†
4-Cl	A	52	1 : 4	45-6°		†
"	B	42	~100% cis	oil		†
4-Br	A	27	<1 : 3		81°	61
"	B	64	~100% cis	oil		
4-CN	A	11	10 : 1	oil	47.5°	62
	C		1 : 6	100-5°	86°	62
4-NO_2	A	35	~100% cis	45-7°	48-9°	60
	C		1 : 1	49-110°	160°	60

* See text

† Not known previously

The β-bromostyrenes which were new compounds were:

3-fluoro-β-bromostyrene; Analysis: C, 47.47; H, 3.49%. C_8H_6BrF requires C, 47.78, H, 3.01%.

3 Chloro-β-bromostyrene; Analysis: C, 44.44, H, 2.74%, C_8H_6BrCl requires C, 44.18; H, 2.78%.

3 Bromo-β-bromostyrene; Found M^+ 259.8838. $C_8H_6Br_2$ requires 259.8837. Repeated elemental analysis failed to yield a satisfactory result.

3-Cyano-β-bromostyrene; Analysis: C, 51.91; H, 3.13%. C_9H_6BrN requires C, 51.95; H, 2.91%.

4-fluoro-β-bromostyrene; Analysis: C, 47.81; H, 2.95%. C_8H_6BrF requires C, 47.78; H, 3.01.

4-chloro-β-bromostyrene; Analysis: C, 43.74; H, 2.76%. C_8H_6BrCl requires C, 44.17; H, 2.78%.

BENZALACETONES

The benzalacetones were prepared by the condensation of acetone with the appropriately substituted benzaldehyde using one of five slightly different experimental procedures.[63] These methods are described below. Yields were normally in the 60-90% range.

Method A[64]

The benzaldehyde (0.2 mole) was mixed with 40 mL acetone (AnalaR). To this was added 5 mL of 10% aqueous sodium hydroxide solution dropwise while cooling in a water bath. The temperature was maintained between 25 and 31^{o} C. The solution was stirred at room temperature for 2 h then 1 M hydrochloric acid added until the mixture was just acid to litmus. At this point two phases separated out. The lighter organic phase was collected and the aqueous phase extracted with benzene. The benzene extracts and the original organic phase was combined, washed with water and the solvent removed by distillation under reduced pressure. This left the crude benzalacetone which was purified by distillation under reduced pressure.

This method was used for the unsubstituted compound and the 3-CH_3, 4-CH_3, 3-OCH_3 and 4-OCH_3 derivatives.

Method B[63]

The benzaldehyde (0.12 mole), 75 mL acetone (AnalaR) and 500 mL water were vigorously stirred at room temperature.

60 mL of a 10% aqueous sodium hydroxide solution was then added dropwise over a period of 1 h. Stirring was continued at room temperature for a further 24 h. The mixture was then extracted with ether and the extracts combined, washed with water and dried over anhydrous magnesium sulphate. The ether was evaporated to leave the crude benzalacetone which was purified by distillation under reduced pressure or recrystallization from ethanol.

This method was used for the 3-F, 3-Cl, 3-Br, 3-CF_3 and 3-CN derivatives.

Method C[65]

Aqueous sodium hydroxide (25 mL of 0.2 M) was added to a cooled solution of 0.03 mole substituted benzaldehyde in 10 mL acetone at such a rate that the temperature stayed below 0^{o} C. After the addition was complete the solution was stirred vigorously for 20 minutes then made slightly acid with concentrated hydrochloric acid. It was then evaporated and the liquid residue heated for 30 minutes at 100^{o} C with 0.5 mL concentrated hydrochloric acid. After cooling the residue was dissolved in hot ethanol, and the crude benzalacetone was deposited as crystals when the alcoholic solution cooled. The crude β-acetyl-styrene was then purified by recrystallization from ethanol.

This method was used for the 3- and 4-NO_2 derivatives.

Method D[66]

A solution of 0.3 g sodium hydroxide in 175 mL ethanol, 40 mL acetone (AnalaR) and 230 mL water was added dropwise with stirring to 0.07 mole of substituted benzaldehyde. The solution was stirred for a further 12 h after the addition and was then filtered to remove any bis-benzalacetone which had precipitated. The filtrate was concentrated to half its original volume causing a second phase to separate out. The new heavier phase solidified on cooling and was recrystallized from ethanol to give the required benzalacetone.

This method was used for the 4-F, 4-Cl and 4-Br derivatives.

Method E[67]

Sodium hydroxide (2.4 g) was dissolved in water (20 mL), 13 mL ethanol and 15 mL acetone (AnalaR). The solution was cooled in an ice water bath to around 3^{o} C. The substituted benzaldehyde (0.04 mole) was added and the mixture stirred for a further 2 h at 3^{o} C. The precipitated benzalacetone was removed by filtration and washed with water until the washings were neutral to litmus. The washing was then completed with a little chilled ethanol.

This method was used only for the 4-dimethylamino derivative.

All of the benzalacetones prepared, except the 3-CF_3 derivative, have been previously described in the literature. 3-Trifluoromethylbenzalacetone was obtained as a colourless liquid, b.p. 72^{o}/2 mm.

Analysis: C,61.8; H, 4.9. $C_{11}H_9F_2O$ requires: C, 61.7; H, 4.6.

ETHYL β-METHYLSULPHONYL CINNAMATES

The ethyl β-methylsulphonyl cinnamates were prepared by condensation of the appropriate benzaldehyde with ethyl methylsulphonyl acetate.[68] Ethyl methylsulphonyl acetate was prepared according to the method of Huppatz.[69] Each of the β-methylsulphonyl cinnamates was prepared by almost exactly the same method. The only variation found to be necessary was a variation in reaction time. For the electron-withdrawing substituents a shorter reaction time was necessary to obtain the required product. A general experimental procedure is described below and Table E-5 gives experimental details for each member of the series.

Preparation of an Ethyl β-methylsulphonyl Cinnamate[68]

Ethyl methylsulphonyl acetate (12 mmol) and the substituted benzaldehyde (12 mmol) were heated under reflux in benzene (8 ml) containing piperidine (0.05 ml) and acetic acid (0.15 ml). The water formed was collected in a Dean and Stark trap and the reaction was usually complete in 2-3 h. The solution was cooled, washed with 0.1 M hydrochloric acid and water. It was dried over anhydrous magnesium sulphate and then the benzene removed by distillation under reduced pressure. The initial product was generally an oil which crystallized on standing. Further purification was by recrystallization from ethanol, vacuum distillation, or in some cases by preparative TLC on silica, or by preparative HPLC.

Table E-5 Experimental Details for the Preparation of a Series of Ethyl β-methylsulphonyl Cinnamates

Ring substituent	Reaction time	Yield(%)*	m.p.	Analysis (Found)		Analysis (Calc.)	
H	2 h	50	53-5°	C=56.77	H=5.69	C=56.68	H=5.55
3-CH_3	2 h	60	58-9°	C=58.01	H=6.03	C=58.19	H=6.01
3-OCH_3	2 h	95	oil	C=54.82	H=5.71	C=54.92	H=5.67
3-F	2.5 h	68	oil	C=52.82	H=5.18	C=52.73	H=4.81
3-Cl	2.5 h	65	55-6°	C=49.93	H=4.61	C=49.42	H=4.54
3-Br	2.5 h	75	73-4°	C=43.00	H=4.04	C=43.26	H=3.93
3-CF_3	30 min	40	71.5-72.5°	C=48.46	H=4.30	C=48.44	H=4.06
3-CN	1.5 h	54	oil	C=56.17	H=5.07	C=55.89	H=4.69
3-NO_2	15 min	30	110-11°	C=48.36	H=4.51	C=48.16	H=4.38
4-$N(CH_3)_2$	3 h	50	131°	C=56.53	H=6.53	C=56.55	H=6.44
4-OCH_3	3 h	65	oil	C=54.69	H=5.72	C=54.92	H=5.67
4-CH_3	3 h	70	87-9°	C=58.42	H=6.22	C=58.19	H=6.01
4-F	2 h	85	80-1°	C=53.06	H=5.03	C=52.93	H=4.81
4-Cl	2 h	70	118-9°	C=49.84	H=4.81	C=49.92	H=4.54
4-Br	2 h	90	128-9°	C=43.42	H=4.29	C=43.26	H=3.93
4-NO_2	10 min	39	90-1°	C=49.20	H=4.85	C=48.16	H=4.38

* Based on their conversion to trans-methyl styryl sulphones it was assumed that in all of the compounds the aromatic ring and the methylsulphonyl group were trans to one another.

METHYL STYRYL SULPHONES

The methyl styryl sulphones were prepared by a dealkylation/decarboxylation of the previously prepared ethyl β-methylsulphonyl cinnamates using lithium iodide in dimethylformamide.[70] The unsaturated sulphone (1.2 m mole) and 0.25 g lithium iodide were refluxed in 10 mL dimethylformamide under an atmosphere of nitrogen for 2 h (less for some compounds). The reaction solution was then poured into water and acidified with dilute hydrochloric acid. The aqueous mixture was extracted with ether and the combined extracts washed with water, dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure. The crude product was purified by column chromatography on alumina, eluting initially with ether and then with chloroform. Further purification by preparative HPLC was necessary for the 3-methoxy and 3-bromo derivatives.

The experimental details for the preparation of this series are contained in Table E-6. (Yields quoted are based on the ethyl β-methylsulphonyl cinnamates).

Many of the methyl styryl sulphones prepared had been previously reported in the literature. Microanalyses for the new compounds are reported below.

Methyl 3-methoxystyryl sulphone, analysis: C, 57.01; H, 5.66%. $C_{10}H_{12}O_3S$ requires C, 56.58; H, 5.70%.

Methyl-3-fluorostyryl sulphone analysis: C, 53.73; H, 4.73%; $C_9H_9FO_2S$ requires C, 53.99; H, 4.53%.

Methyl-3-chlorostyryl sulphone analysis: C, 49.61; H, 4.30%; $C_9H_9ClO_2S$ requires C, 49.89; H, 4.19%.

Methyl-3-bromostyryl sulphone, found $M^{+\cdot}$ 259.9505. $C_9H_9BrO_2$ requires 259.9507. Repeated elemental analysis failed to give a satisfactory result.

Methyl 3-trifluoromethyl styryl sulphone, analysis: C, 47.92, H, 3.98%, $C_{10}H_9F_3O_2S$ requires C, 47.99; H 3.63%.

Methyl 3-cyanostyryl sulphone, analysis: C, 57.52; H, 4.79%, $C_{10}H_9NO_2S$ requires C, 57.95, H, 4.38%.

Methyl 4-methyl styryl sulphone, analysis: C, 60.89; H, 6.40%, $C_{10}H_{12}O_2S$ requires C, 61.20; H, 6.16%.

Methyl 4-fluoro styryl sulphone, analysis C, 53.87; H, 4.72% $C_9H_9FO_2S$ requires C, 53.99; H, 4.53%.

Methyl-4-bromo styryl sulphone, analysis C, 41.49; H, 3.72% $C_9H_9BrO_2S$ requires C, 41.39; H, 3.47%.

^{13}C NMR spectra for the 3-NO_2 4-Cl, H, 4-CH_3, 4-F and 4-OMe derivatives compare well with the ^{13}C data for these compounds given in Ref. 28.

Table E-6 Experimental Details for the Preparation of a Series of Methyl Styryl Sulphones.

Substituent	Reaction time (h)	Yield	Physical appearance
H	1	73%	White crystals m.p. 77-78° C (lit.[71] 80° C)
3-Me	2	86%	Pale yellow oil
3-MeO	2	84%	Colourless oil
3-F	2	78%	White crystals m.p. 91-92° C
3-Cl	2	80%	White crystals m.p. 72-73° C
3-Br	2	90%	White crystals m.p. 60-61° C
$3-CF_3$	0.5	58%	White crystals m.p.107-108° C
3-CN	0.5	50%	White crystals m.p.109-110° C
$3-NO_2$	2	60%	Orange crystals m.p. 114-116° C
4-Me	2	85%	White crystals m.p. 109-110° C
4-MeO	3	84%	Orange crystals m.p.138-140° C (lit.[71] 143-144)
4-F	2	85%	White crystals m.p. 128-129° C
4-Cl	2	97%	White crystals m.p. 127-128°C (lit.[71] 128-129°C)
4-Br	3	77%	White crystals m.p. 134°C

CINNAMONITRILES

The cinnamonitriles were prepared by a decarboxylation of the β-cyano cinnamic acids, prepared in turn by the condensation of benzaldehydes with sodium cyanoacetic acid in aqueous potassium hydroxide solution.

Preparation β-Cyano Cinnamic Acids[29]

Cyanoacetic acid (8 m mole) was dissolved in 7 mL of a 2.5 M aqueous solution of potassium hydroxide. The substituted benzaldehyde (8 m mole) was added and the mixture warmed to 40° C and kept at this temperature for 1 h. The mixture was acidified with concentrated hydrochloric acid and allowed to stand for 1 h. The β-cyanocinnamic acid was filtered from the solution, washed with water, air-dried, washed with petroleum ether and air-dried. No further purification was necessary. Yields were generally 80-90%.

The decarboxylation was carried out by either of two methods.

Method A. β-Cyanocinnamic acid (5 m mole), and a catalytic amount of copper sulphate were refluxed in pyridine for 3 h. Most of the pyridine was then removed by distillation under reduced pressure and the residue taken up in ether. The ether solution was washed with 6 M hydrochloric acid (5X) and water. It was then dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure. The crude product was purified by column chromatography on alumina, eluting with ether/petroleum ether mixtures.

Method B.[29] The β-cyanocinnamic acid (5 m mole) was heated with cuprous oxide (0.1 g) under a vacuum of about 1 mm. The cinnamonitrile distilled from the mixture and was purified by column chromatography.

In some cases the substituted benzaldehyde was condensed with cyanoacetic acid by refluxing for six hours in pyridine solution. In these circumstances the β-cyanocinnamic acid was decarboxylated as it formed and was not isolated.

In all cases the cinnamonitriles were prepared as mixtures of the cis and trans isomers. No effort was made to separate these isomers. In the case of 4-methyl-cinnamontrile, column chromatography happened to produce a pure sample of the trans isomer.

The individual experimental details for the preparation of the cinnamonitrile series are summarized in Table E-7.

Table E-7 Experimental details for the Preparation of a series of Cinnamonitriles

Substituent	Yield of β-cyanocinnamic acid	Method of Decarboxylation	Yield of cinnamonitrile	Cis/trans ratio	Physical appearance
H	97%	A	85%	2 : 5	Pale yellow
3-Me	95%	A	77%	2 : 3	Colourless oil
3-MeO	not isolated*	A	51% (based on Aldehyde)	1 : 1	Colourless oil
3-F	not isolated*	A	50% (based on Aldehyde)	2 : 3	Pale yellow oil
"	34%	B	78%	1 : 1	Crystals in brown oil
3-Cl	not isolated*	A	55% (based on Aldehyde)	2 : 5	Yellow oil
3-Br	81%	A	91%	1 : 5	Crystals in light brown oil
$3-CF_3$	54%	A	90%	1 : 2	Crystals in light brown oil
3-CN	not isolated*	A	41% (based on Aldehyde)	1 : 2	Crystals in yellow oil
$3-NO_2$	not isolated*	A	15% (based on Aldehyde)	2 : 3	Orange oil
4-Me	77%	A	20%	~100% trans	Cream cyrstals p.m. 72-75° C (lit.[29] 73-76° C)
"		B	75%	5 : 1	Crystals in orange oil
4-MeO	74%	A	30%	1 : 2	Orange oil
$4-NMe_2$	75%	B	50%	1 : 10	Orange crystals
4-F	90%	A	39%	1 : 25	White crystals
"		B	52%	3 : 2	Yellow crystals
4-Cl	60%	A	76%	2 : 3	Orange crystals
4-Br	not isolated*	A	89%	1 : 1	Pale yellow oil
$4-NO_2$	90%	A	20%	1 : 2	Brown crystals

* Decarboxylation occurred during the reaction. Only the cinnamonitrile could be isolated.

METHYL CINNAMATES

Most of the methyl cinnamates were prepared by esterification of the appropriately substituted cinnamic acid. Table E-8 contains a summary of the experimental details for these preparations. Many of the cinnamic acids were available having been used previously for the β-bromostyrene syntheses.

Methyl 3-dimethylaminocinnamate was prepared by methylation of meta-aminocinnamic acid followed by esterification.

The meta- and para-bromomethyl substituted compounds were made from the methyl meta- and para-methylcinnamates by a Wohl-Ziegler bromination.[51] The experimental procedures for these preparations are outlined below.

The remainder of the $-CH_2X$ substituted methyl cinnamates were prepared from the bromomethyl derivatives by nucleophilic substitution under a variety of reaction conditions. The individual experimental procedures are given in the following.

Methyl 3-dimethylaminocinnamate[72]

3-Aminocinnamic acid (750 mg) was stirred in 2 mL water. 1.74 g dimethylsulphate was added in 3 equal portions. After the first addition the mixture was allowed to stand until homogeneous. The solution was then carefully neutralised with 25% potassium hydroxide solution while cooling in an icebath. The second portion of dimethyl sulphate was added and the process repeated except that a slight excess of

the potassium hydroxide solution was added. After the addition of the third portion of dimethylsulphate the solution was allowed to stand for one hour.

At this point most of the water was removed by evaporation under reduced pressure. The residue was dissolved in 20 mL methanol and 0.5 mL concentrated sulphuric acid was added. The mixture was refluxed for 2 h then concentrated to half its volume. A slight excess of a saturated solution of sodium carbonate was added and the aqueous mixture extracted with ether. The combined extracts were washed with water then dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to leave 40 mg (4%, based on 3-amino cinnamic acid) of yellow crystals. The crude product was purified by preparative HPLC to give white crystals which rapidly turned a lemon colour m.p. 56-58^{o} C.
Found: $M^{+\cdot}$, 205.112; C, 69.90%, H, 7.52%; $C_{12}H_{15}NO_2$ requires; $M^{+\cdot}$, 205.110, C, 70.22%; H, 7.37%.

Methyl 3-bromomethylcinnamate

Methyl 3-methylcinnamate (39 g), N-bromosuccinimide (46 g) and dibenzoyl peroxide (5 g) were refluxed in 100 mL carbon tetrachloride for 90 minutes. The cooled solution was filtered under suction and the solvent removed from the filtrate by distillation under reduced pressure. Proton NMR of the crude product (a yellow oil) showed it to contain about equal quantities of the methyl 3-methylcinnamate and the required product. Neither extending the reaction time nor increasing the molar ratio of N-bromosuccinimide improved the yield. The crude product was distilled rapidly under

reduced pressure. The methyl 3-bromomethylcinnamate was collected in a fraction boiling at 160°C/0.1 mm. However much of the material was lost by decomposition in the distillation flask. The product was recrystallized from ether to yield 8.5 g (15%, based on methyl 3-methylcinnamate) white crystals m.p. 81-82°C.

Analysis: C, 51.53; H, 4.67%; $C_{11}H_{11}BrO_2$ requires C, 51.79, H, 4.35%.

Methyl 4-bromomethylcinnamate

Methyl 4-methylcinnamate (17 g), N-bromosuccinimide (20 g) and dibenzoyl peroxide (2 gm) were refluxed in 80 mL carbon tetrachloride for 45 minutes. The cooled solution was filtered and the solvent removed from the filtrate by distillation under reduced pressure. The crude product was a yellow oil which crystallized on standing. Proton NMR indicated that methyl 4-methylcinnamate (the starting material) was only present as a minor impurity. Recrystallization from an ether/petroleum ether mixture gave 10 g (41%, based on methyl 4-methylcinnamate) of white crystals, m.p. 59-60° C. ^{1}H NMR(δ): 3.8 s(CH_3), 4.45 s(CH_2), 7.2-7.8 m (C_6H_4), 6.35 and 7.6 (CH=CH system, J = 16 Hz).

Methyl 3-chloromethylcinnamate

Methyl 3-bromomethylcinnamate (250 mg) and lithium chloride (330 mg) were stirred in 5 mL dry dimethyl sulphoxide at room temperature for 12 h. The DMSO solution was poured into water and extracted with chloroform. The combined extracts were washed with water then dried over

anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to leave 180 mg of methyl 3-chloromethylcinnamate (87% based on methyl 3-bromomethylcinnamate) a pale yellow oil which crystallized on standing. The product was recrystallized from petroleum ether to give white crystals m.p. 62-63° C.
Analysis: C, 62.62; H, 5.32%. $C_{11}H_{11}ClO_2$ requires C, 62.72, H, 5.26%.

Methyl 4-chloromethylcinnamate

This was prepared from the methyl 4-bromomethylcinnamate in exactly the same way that was decribed for the preparation of methyl 3-chloromethylcinnamate from the 3-bromomethyl derivative. The yield was 85%, based on methyl 4-bromomethylcinnamate. The product was recrystallised from petroleum ether to give white crystals m.p. 34°C.
Analysis: C, 62.83; H, 5.31%. $C_{11}H_{11}ClO_2$ requires C, 62.72; H, 5.26%.

Methyl 3-iodomethylcinnamate

Methyl 3-bromomethylcinnamate (500 mg) was stirred at room temperature with 1.0 g sodium iodide in 10 mL acetone for 12 h. The reaction solution was poured into water and the resulting suspension extracted with chloroform. The combined extracts were washed with a 0.5 M aqueous solution of sodium thiosulphate, and with water before drying over anhydrous magnesium sulphate. The solvent was removed under reduced pressure to leave 480 mg (81%, based on methyl 3-bromomethylcinnamate) of yellow crystals.

The product was recrystallized from an ether/petroleum ether mixture to give cream crystals m.p. 95-96° C. The crystals darkened rapidly and the microanalysis was consistent with some loss of iodine.

Found: $M^{+\cdot}$, 301.990; C, 45.43%, H; 4.42. $C_{11}H_{11}IO_2$ requires $M^{+\cdot}$, 301.981; C, 43.72%; H, 3.67%.

Mass spectrum shows a very strong peak at mass 175 corresponding to loss of $I^{-\cdot}$ and only a weak peak for the molecular ion.

Methyl 3-Fluoromethylcinnamate[73]

Methyl 3-bromomethylcinnamate (500 mg) and 1.0 g of anhydrous potassium fluoride (dried by heating for 12 h at 200° C/.1 mm in a drying pistol with potassium hydroxide pellets as a desiccant) were refluxed together for 7 h in 15 mL dry N-methyl pyrollidone (dried by distillation from potassium hydroxide). The reaction solution was cooled and poured into a saturated solution of ammonium chloride. The product was extracted with ether. The combined extracts were washed with saturated ammonium chloride solution and with water. The ether solution was dried over anhydrous magnesium sulphate and evaporated to yield 370 mg (84%, based on methyl 3-bromomethylcinnamate) of pale yellow oil. This was purified by column chromatography on 30 mls florisil. The pure fluoromethyl derivative was contained in a fraction eluted with 5% ether/petroleum ether and was a colourless oil. Analysis: C, 68.04; H, 5.93%. $C_{11}H_{11}FO_2$ requires C, 68.02, H, 5.71%.

Methyl 4-fluoromethylcinnamate

Methyl 4-fluoromethylcinnamate was prepared in the same way as described for the methyl 3-fluoromethylcinnamate. The yield, based on methyl 4-bromomethylcinnamate, was 87%. The product was purified by recrystallization from petroleum ether to give white crystals m.p. 49-50° C.
Analysis: C, 67.58; H, 6.01%. $C_{11}H_{11}FO_2$ requires C, 68.02; H, 5.71%.

Methyl 3-cyanomethylcinnamate

Methyl 3-bromomethylcinnamate (250 mg) and 100 mg sodium cyanide were stirred in 10 mL dry DMSO for 20 minutes. The solution was poured into water and the aqueous mixture extracted with chloroform. The combined extracts were washed (6x) with water, dried over anhydrous magnesium sulphate, and the solvent removed by distillation under reduced pressure to leave 160 mg (81%, based on methyl 3-bromomethylcinnamate) of yellow oil which crystallized on standing. The product was recrystallized from an ether/petroleum ether mixture to give white crystals m.p. 73-74° C.
Analysis: C, 71.53; H, 5.59%. $C_{12}H_{11}NO_2$ requires C, 71.62; H 5.51%.

Methyl 4-cyanomethylcinnamate

Methyl 4-cyanomethylcinnamate was prepared by a method analogous to that for the 3-cyanomethyl derivative. The yield based on methyl 4-bromomethylcinnamate was 69%. The product was recrystallized from an ether/petroleum ether mixture to give cream crystals m.p. 77-79° C. These

crystals were further purified by HPLC to give white crystals m.p. 78-79° C.

Analysis: C, 71.63; H, 5.82%. $C_{12}H_{11}NO_2$ requires C, 71.62; H, 5.51%.

Methyl 3-nitromethylcinnamate [74]

Methyl 3-bromomethylcinnamate (300 mg) in anhydrous ether (5 mL) was added over 3 h to a stirred slurry of silver nitrite (1 g) and calcium hydride (100 mg) in anhydrous ether. During the addition and the remainder of the reaction, the whole system was kept in the dark and at a temperature of about 3° C. The mixture was stirred for a further 200 h. After this time the mixture was filtered under suction and the solids washed with more ether. The combined washings and original filtrate were evaporated to give 220 mg (85%, based on methyl 3-bromomethylcinnamate) of white crystals. The product was recrystallized from methanol/water to give white crystals m.p. 86-87°C.

Analysis: C, 59.61; H, 5.29%. $C_{11}H_{11}NO_4$ requires C, 59.72; H, 5.01%.

Methyl 4-nitromethylcinnamate

Methyl 4-nitromethylcinnamate was prepared by a method analogous to that described for the 3-nitromethyl derivative. The yield, based on methyl 4-bromomethyl-cinnamate was 81%. The product was recrystallized from ether/petroleum ether solution to give white crystals m.p. 102°C.

Analysis C, 59.83; H, 5.24%. $C_{11}H_{11}NO_4$ requires C, 59.72; H, 5.01%.

Methyl 3-methoxymethylcinnamate

Methyl 3-bromomethylcinnamate (250 mg) was refluxed in 20 mL of methanol for 45 h. The solution was then concentrated to half its volume and poured into water. The aqueous mixture was extracted with ether and the combined extracts washed with water. The ether solution was dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure to leave 145 mg (72% based on methyl 3-bromomethylcinnamate) of yellow oil. This was purified by preparative HPLC to give a colourless oil.

Analysis: C, 69.27; H, 7.14%. $C_{12}H_{14}O_3$ requires C, 69.88; H, 6.84%.

Methyl 4-methoxymethylcinnamate

Methyl 4-methoxymethylcinnamate was prepared by a method analogous to that described for the 3-methoxymethyl derivative. The yield, based on methyl 4-bromomethylcinnamate was 74%. The crude product was purified by HPLC to give a white crystalline solid m.p. 39-40^{o} C.

Analysis: C, 69.48; H, 7.47%. $C_{12}H_{14}O_3$ requires C, 69.88; H, 6.84%.

Methyl 3-phenoxymethylcinnamate

Methyl 3-bromomethylcinnamate (250 mg), 250 mg anhydrous potassium carbonate and 200 mg phenol were refluxed with stirring in 20 mL acetone for 6 h. The solution was then poured into water and the aqueous mixture extracted with ether. The combined extracts were washed (5x)

with a saturated solution of sodium carbonate and washed (4x) with water. The ether solution was then dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure to leave 210 mg (79%, based methyl 3-bromomethylcinnamate) of pale yellow oil which crystallized on standing and was recrystallized from petroleum ether to give white crystals m.p. 81-82° C. Analysis: C, 76.15; H, 6.38%. $C_{17}H_{16}O_3$ requires C, 76.10; H, 6.01%.

Methyl 4-phenoxymethylcinnamate

Methyl 4-phenoxymethylcinnamate was prepared by the same procedure as was described for the 3-phenoxymethyl derivative. The yield, based on methyl 4-bromomethyl-cinnamate was 85%. The product was recrystallized from petroleum ether to give white crystals m.p. 114-116° C. Analysis: C, 76.10; H, 6.42%. $C_{17}H_{16}O_3$ requires C, 76.10; H, 6.01%.

Methyl 3-dimethylaminomethylcinnamate

Methyl 3-bromomethylcinnamate (500 mg) was stirred in 10 mL dry dimethylsulphoxide which had been cooled almost to the point of freezing (~18° C), Dimethylamine (0.5 mL) was added and the cooled solution stirred for 30 minutes. It was then poured into water and the aqueous mixture extracted with ether. The combined ether extracts were washed (4x) with water and dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to leave 370 mg (86%, based on methyl 3-bromo-

methylcinnamate) of colourless oil. This was dissolved in pentane and the pentane solution filtered to remove the more polar impurities which had precipitated. The pentane was removed under reduced pressure at room temperature. Found: $M^{+\cdot}$, 219.128. $C_{13}H_{17}NO_2$ requires $M^{+\cdot}$, 219.126 H^1NMR(δ): 2.20 s ($N(CH_3)_2$, 3.35 s (CH_2), 3.73 (CO_2CH_3), 7.1-7.5 m (C_6H_4), 6.33 and 7.57 (CH=CH system, J=16 Hz). A sample was subjected to an elemental analysis which was unsatisfactory. An elemental analysis of the same sample performed 12 h later gave a carbon content 1% lower still.

Methyl 4-dimethylaminomethylcinnamate

This was prepared in the same manner as was described for the 3-dimethylaminomethyl derivative. The yield was 78%, based on methyl 4-bromomethylcinnamate. The crude product was a pale yellow oil (200 mg, 78%, based on methyl 4-bromomethylcinnamate) and was purified by the method used for the 3-dimethylaminomethyl compound to give a colourless oil.

Found: $M^{+\cdot}$, 219.127. $C_{13}H_{17}NO_2$, requires $M^{+\cdot}$ 219.126 ^{1}HNMR(δ): 2.20 s($N(CH_3)_2$), 3.35s(CH_2), 3.73 s(CO_2CH_3), 7.1 - 7.5 m (C_6H_4), 6.30 and 7.55 (CH = CH system, J = 16 Hz).

Table E-8 Preparations of Methyl Cinnamates*

Substituent	Yield(%)†	m.p.(expt.)	m.p.(lit.)	Ref.
3-Me	93	30-2°	32-3°	75
3-OMe	93	oil		
3-OPh	78	oil		
3-F	96	oil	b.p.124-8°/ 11 mm	76
3-Br	85	51-4°	55-6°	77
3-I	96	55-7°	55-7°	78
3-CN	93	94-6°		79
3-NO_2	95	123-4°	123-4°	80
4-Me	67	46-8°	49-50°	75
4-OPh	84	81-2°	79-9.5°	81
4-F	92	45-6°		
4-Br	96	91-3°	96-7°	77
4-I	81	129-30°		

* The unsubstituted compound was available commercially. The 3-Cl, 3-CF_3, 4-OMe, 4-NMe_2, 4-Cl, and 4-NO_2 derivatives were available within the department. The preparation of the other cinnamates used is described in the text.

† All derivatives except one were prepared by the esterification of the appropriate cinnamic acid. This (the 3-NMe_2 compound) was prepared indirectly from the 3-aminocinnamic acid by methylation and esterification.

Of the methyl cinnamates referred to in Table E-8 three have not previously been reported in the literature. These are methyl 4-fluorocinnamate (Analysis: C, 66.97%; H, 5.33%. $C_{10}H_9FO_2$ requires C, 66.66%; H, 5.04%), Methyl 4-iodocinnamate (Analysis: C, 41.86; H, 3.64. $C_{10}H_9IO_2$ requires C, 41.69%; H, 3.25%) and methyl 3-phenoxycinnamate. (Found $M^{+\cdot}$ 254.0977. $C_{16}H_{14}O_3$ requires 254.0943.)

FLUOROBENZENES

The 3- and 4-fluorobenzyl derivatives were prepared by nucleophilic substitution on the 3- and 4-fluorobenzyl bromides. The exceptions however, were the 3- and 4-ethylfluorobenzenes which were prepared by Wolff-Kishner reductions[53] of 3- and 4-fluoroacetophenones. The fluorobenzyl derivatives were all liquids and have all been previously reported in the literature. The success of each preparation was confirmed by the proton NMR spectrum of the product.

Both the meta- and para-fluorobenzyl derivatives were prepared by the same method. Only the preparations of the meta-fluorobenzyl derivatives will be described here.

Preparation of Precursors

3-Fluorobenzylbromide and 3-fluoroacetophenone were commercially available and were used without further purification. 4-Fluorobenzylbromide was made[51] from 4-fluorotoluene and 4-fluoroacetophenone was prepared from fluorobenzene by a Friedel-Crafts acylation.[82]

4-Fluorobenzylbromide

4-Fluorotoluene (15 g), N-bromosuccinimide (24.6 g) and dibenzoyl peroxide (5 g) were refluxed with stirring in 115 mL carbon tetrachloride for 30 minutes. The cooled solution was filtered under suction and the solvent removed by distillation under reduced pressure leaving a pale yellow liquid (25 g). The crude product was

distilled under reduced pressure to give 19 g (74%, based on 4-fluorotoluene) of 4-fluorobenzyl bromide as a colourless liquid b.p. 55° C/0.2 mm. ^{1}H NMR(δ): 4.40 s ($-CH_2-$), 6.6-7.6 m (C_6H_4).

4-Fluoroacetophenone[82]

Aluminium chloride (18.5 g) and 30 g fluorobenzene were stirred in a flask cooled in a cold water bath. Redistilled acetic anhydride (6.4 g) was added dropwise over 15 minutes. After the addition the mixture was refluxed on a steam bath for 30 minutes. It was then allowed to cool and poured with stirring into a mixture of 40 g ice and 40 mL concentrated hydrochloric acid. The aqueous solution was stirred until all the aluminium salts dissolved and was then extracted with ether. The combined extracts were washed with a 10% solution of sodium hydroxide and with water. The ether solution was dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure to leave a dark orange oil. This was distilled at atmospheric pressure to give 1.9 g (31%, based on fluorobenzene) of 4-fluoroacetophenone, b.p. 198° C/ 760 mm.

3-Ethylfluorobenzene[53]

Potassium hydroxide (1.2 g) was dissolved in 3 mL ethylene glycol. Hydrazine hydrate (1.4 mL of 98-100%) and then 500 mg 3-fluoroacetophenone were added. The mixture was stirred under reflux for 1 h. The condenser was then set up for distillation and the heating and stirring continued. Once the 3-fluoro-ethylbenzene and water stopped distilling,

the reaction solution was allowed to cool and 10 mL of water added. This was distilled from the solution and added to the first distillate. The total distillate was then extracted with ether. The combined extracts were washed with water and dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to yield 420 mg (93%, based on 3-fluoroacetophenone) of 3-fluoro-ethylbenzene. ^{1}H NMR δ: 1.10 t(CH_3, J = 6.0 Hz), 2.60 q (CH_2, J = 7.0 Hz); 6.6 - 7.6 m (C_6H_4).

3-Fluorobenzyl methyl ether

3-Fluorobenzyl bromide (1.0 g) was refluxed in methanol (15 mL) for 18 h. The solution was then diluted to 30 mL with water and extracted with ether. The combined extracts were washed with water and dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to leave 0.66 g (89%, based on 3-fluorobenzyl bromide) 3-fluorobenzyl methyl ether as a pale yellow oil. ^{1}H NMR(δ) : 3.33 s (CH_3); 4.40 s (CH_2), 6.6 - 7.6 m (C_6H_4).

3-Fluorobenzyl phenyl ether

3-Fluorobenzyl bromide (600 mg), phenol (350 mg) and potassium carbonate (450 mg) were refluxed with stirring in 10 mL acetone for 3 h. The reaction mixture was diluted with 20 mL water and extracted with ether. The combined extracts were washed with a saturated solution of sodium carbonate and with water. The ether solution was dried

over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure to leave 460 mg (72%, based on 3-fluoro benzyl bromide) of 3-fluorobenzyl phenyl ether as a pale yellow oil. ^{1}H NMR(δ): 4.97 s (CH_2); 6.6-7.6 m (C_6H_4 and OC_6H_5).

3-Fluoro-N,N-dimethylbenzylamine.

3-Fluorobenzyl bromide (500 mg) was stirred for 20 minutes in 25 mL of a 40% aqueous solution of dimethylamine. The reaction mixture was then made slightly alkaline with sodium hydroxide and extracted with ether. The combined extracts were washed with water, dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure to leave 330 mg (82%, based on 3-fluorobenzyl bromide of 3-fluoro-N,N-dimethyl benzylamine as a pale yellow liquid. ^{1}H NMR(δ) : 2.1 s (CH_3); 3.3 s (CH_2); 6.6-7.6 m (C_6H_4).

3-Fluorobenzyl fluoride[73]

Anhydrous potassium fluoride (1.0 g dried by heating for 12 h at 200°C/0.1 mm in a drying pistol using potassium hydroxide pellets as a desiccant) was stirred vigorously in 15 mL N-methyl pyrrolidone at about 120° C. 3-Fluorobenzyl bromide (1 g) was then added dropwise over the period of 10 minutes. Stirring and heating was continued for a further two and a half hours. The solution was then allowed to cool and poured into a saturated solution of ammonium chloride. The mixture was extracted with ether. The combined extracts were dried over anhydrous

magnesium sulphate and the solvent removed by distillation under reduced pressure to leave 580 mg (86%, based on 3-fluorobenzyl bromide) of a dark orange oil. This crude product was purified by distillation under reduced pressure. 3-Fluorobenzyl fluoride had b.p. 60° C/100 mm. ^{1}H NMR(δ): 5.73 d (CH_2, J_{HF}=48 Hz); 6.6 - 7.6 m (C_6H_4).

3-Fluorobenzyl chloride

3-Fluorobenzyl bromide (500 mg) and lithium chloride (500 mg) were stirred at room temperature for 17 h in 10 mL dry dimethyl sulphoxide. The solution was poured into water and the aqueous mixture extracted with ether. The combined extracts were washed with water, dried over anhydrous magnesium sulphate and the solvent removed by distillation under reduced pressure to yield 330 mg (86%, based on 3-fluoro benzylbromide) of 3-fluorobenzyl chloride as a colourless liquid. ^{1}H NMR(δ): 4.47 s (CH_2); 6.4-7.6 m (C_6H_4).

3-Fluorobenzyl iodide

3-Fluorobenzyl bromide (500 mg) and sodium iodide (1 g) were stirred for 15 h in 10 mL acetone at room temperature. The reaction solution was diluted to twice its original volume with water and extracted with ether. The combined extracts were washed with 0.5 N sodium thiosulphate solution, washed with water then dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to leave 510 mg (82% based on 3-fluorobenzyl bromide) of 3-fluorobenzyl iodide

as a yellow liquid which rapidly darkened to a deep red. ^{1}H NMR(δ): 4.30 s (CH_2); 6.4-7.6 m (C_6H_4).

3-Fluorobenzyl cyanide

3-Fluorobenzyl bromide (500 mg) and sodium cyanide (300 mg) were stirred in 10 mL dry dimethyl sulphoxide at room temperature for 80 minutes. The solution was poured into water and extracted with ether. The combined extracts were washed with water and dried over anhydrous magnesium sulphate. The solvent was removed by distillation under reduced pressure to yield 310 mg (87%, based on 3-fluorobenzyl bromide) of 3-fluorobenzyl cyanide as a pale yellow liquid. ^{1}H NMR(δ): 3.67 s (CH_2); 6.2-7.8 m (C_6H_4).

3-Fluorophenylnitromethane[74]

A slurry of 1 g silver nitrite and 0.1 g calcium hydride in 2.5 mL dry ether was stirred and cooled to below 0^{o} C in an ice/salt bath. 3-Fluorobenzyl bromide (1 g) was added dropwise to the slurry over 15 minutes. The mixture was stirred for a further 15 h at 3^{o} C in the dark. The solid was then removed by filtration and washed with more ether. The original filtrate and the washings were combined and evaporated to yield 720 mg (88%, based on 3-fluorobenzyl bromide of crude 3-fluorophenylnitromethane. This was purified by liquid chromatography on a column of 30 mL silica-gel eluting with petroleum ether/ether mixtures. The pure 3-fluorophenylnitromethane was contained in a fraction eluted with

10% ether/petroleum ether and was a colourless oil.

^{1}H NMR(δ): 5.32 s (CH_2); 6.4-7.6 m (C_6H_4).

RESULTS

Tables R-1 to R-9 list the ^{13}C NMR chemical shifts (quoted in ppm downfield from tetramethylsilane) for all the carbons in the eight series of substituted styrenes prepared. The missing chemical shifts correspond to quaternary carbons whose long relaxation times resulted in peaks of too low intensity to be observed.

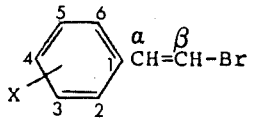
Table R-10 lists the ^{13}C NMR substituent chemical shifts for the β-side-chain carbon of the methyl cinnamates. The data is given for spectra recorded in six solvents.

Table R-11 is analogous to table R-10 except that it lists the ^{13}C NMR substituent chemical shifts for the α-side-chain carbon of the methyl cinnamates.

Tables R-12 and R-13 list the ^{19}F NMR chemical shifts for the 3-fluorobenzyl and 4-fluorobenzyl derivatives respectively, in five solvents.

The experimental uncertainty for the ^{13}C NMR data was estimated to be about ± 0.05 ppm. For the ^{19}F NMR data of Table R-12 the estimated uncertainty is ± 0.03 ppm and for the ^{19}F data of Table R-13 it is even better at ± 0.01 ppm.

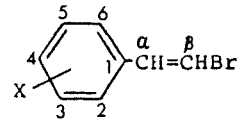
Table R-1

trans-β-bromostyrenes 

Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	Other
H	135.96	126.10	128.78	128.25	128.78	126.10	137.18	106.51	
3-Me	135.91	126.84	138.37	129.04	128.65	123.28	137.29	106.23	21.28
3-OMe	137.25	111.62	159.90	113.86	129.73	118.69	137.10	106.82	55.21
3-F		112.78 (J=1.16)	163.16 (J=12.32)	115.18 (J=1.07)	130.32 (J=0.42)	122.01 (J=0.14)	136.19 (J=0.13)	108.06	
3-Cl	137.66	126.06	134.81	128.22	129.98	124.25	135.87	108.15	
3-Br	138.12	129.14		131.42	131.23	124.75	135.88	108.23	
3-CF_3	136.71	123.98 (J=0.21)		126.19 (J=0.25)	129.59	129.28	135.89	108.73	
3-CN	137.10	129.68	113.18	131.49	129.50	130.13	135.06	109.63	
3-NO_2	136.57	120.69		122.79	129.82	131.81	135.04	110.14	
4-Me	133.21	126.03	129.49	138.23	129.49	126.03	137.07	105.42	21.25
4-OMe	128.87	127.38	114.26	159.77	114.26	127.38	136.62	104.01	55.28
4-NMe_2		127.15	112.34		112.34	127.15	136.98	101.56	40.37
4-F	131.16 (J=0.24)	127.75 (J=0.41)	115.81 (J=1.08)	162.68 (J=12.41)	115.81 (J=1.08)	127.75 (J=0.41)	136.02	106.11 (J=0.13)	
4-Cl	134.41	127.27	128.99	134.07	128.99	127.27	135.97	107.18	
4-Br	134.80	127.57	131.96	122.20	131.96	127.57	136.04	107.32	
4-CN	140.12	126.59	132.66	111.78	132.66	126.59	135.71	110.84	
4-NO_2		126-52	123.52		123.52	126.71	135.37	111.65	

Table R-2

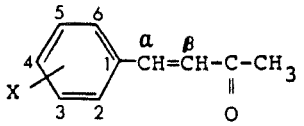
cis-β-bromostyrenes



Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	Other
H	134.96	128.99	128.23	128.01	128.23	128.99	132.36	106.34	
3-Me	134.89	129.68	137.84	129.09	128.14	126.06	132.49	106.08	21.33
3-OMe	136.56	114.32	158.35	113.77	129.19	121.69	132.21	106.49	55.21
3-F	137.08 (J=0.41)	115.65 (J=1.13)	162.65 (J=12.37)	115.26 (J=1.06)	129.73 (J=0.42)	124.96 (J=0.14)	131.40 (J=0.12)	107.73	
3-Cl	136.66	128.84	134.17	128.31	129.46	127.09	131.16	107.93	
3-Br	137.10	131.87	122.41	130.31	129.78	127.56	131.23	108.05	
3-CF_3	135.67	125.76 (J=0.19)		124.92 (J=0.19)	128.75	132.07	131.16	108.49	
3-CN	136.19	132.28	112.66	131.57	129.16	133.15	130.43	109.44	
3-NO_2	134.39	123.68	148.26	122.93	129.25	134.73	130.40	109.81	
4-Me	132.16	128.94	128.94	138.29	128.94	128.94	132.23	105.42	21.35
4-OMe	128.04	130.49	113.64		113.64	130.49	131.66	104.12	55.25
4-F		130.86 (J=0.41)	115.26 (J=1.09)	162.44 (J=12.45)	115.26 (J=1.09)	130.86 (J=0.41)	131.28	106.22 (J=0.09)	
4-Cl	133.39	130.26	128.48	133.39	128.48	130.26	131.26	107.17	
4-Br	133.79	130.51	131.44	122.31	131.44	130.51	131.32	107.31	
4-CN	139.40	129.46	132.02	111.82	132.02	129.46	130.97	110.05	
4-NO_2	141.32	129.71	123.55		123.55	129.71	130.73	110.73	

Table R-3

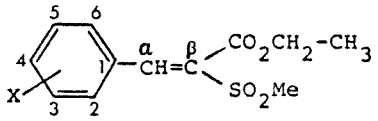
Benzalacetones



Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	$-\overset{\overset{O}{\|}}{C}-$	$-CH_3$	Other
H	134.56	128.29	129.01	130.53	129.01	128.29	143.42	122.26	198.22	27.49	
3-Me	134.51	128.91	138.36	131.38	128.91	125.52	143.62	127.07	198.27	27.46	21.30
3-OMe	135.87	113.12	160.05	116.44	129.98	121.04	143.35	127.48		27.48	55.31
3-F	136.81 (J=0.40)	114.46 (J=1.11)	163.10 (J=12.37)	117.35 (J=1.05)	130.55 (J=0.41)	124.27 (J=0.15)	141.85 (J=0.11)	128.21	197.99	27.69	
3-Cl	136.41	127.98	135.04	130.31	130.22	126.40	141.51	128.24	197.75	27.70	
3-Br	136.67	130.94	123.12	133.23	130.46	126.83	141.43	128.24	197.76	27.74	
3-CF_3	135.37	124.86 (J=0.18)		126.88 (J=0.20)	129.59	131.23	141.39	128.63	194.48	27.81	
3-CN	135.87	131.53	113.51	133.33	129.91	132.06	140.31	129.11	194.72	27.96	
3-NO_2	136.39	122.62		124.67	130.07	133.76	140.15	129.48	197.46	28.03	
4-Me	131.81	128.32	129.77	141.02	129.77	128.32	143.52	126.34	198.35	27.41	21.47
4-OMe	126.94	129.96	114.50	161.67	114.50	129.96	143.19	125.09	198.25	27.37	55.38
4-NMe_2	122.16	130.06	111.94		111.94	130.06	144.32	122.49	198.27	27.13	40.07
4-F	130.77 (J=0.16)	130.18 (J=0.42)	116.18 (J=1.11)	164.10 (J=12.59)	116.18 (J=1.11)	130.18 (J=0.42)	142.03	126.95 (J=0.13)	198.03	27.60	
4-Cl	133.06	129.41	129.30	136.48	129.30	129.41	141.81	127.57	197.88	27.65	
4-Br	133.41	129.56	132.23	124.77	132.23	129.56	141.85	127.59	194.25	27.65	
4-NO_2	140.79	124.25	128.86		128.86	124.25	140.06	130.47	197.41	28.03	

Table R-4

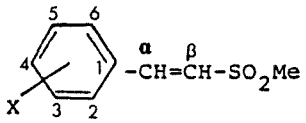
Ethyl-β-Methylsulphonylcinnamates



Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	$-CH_3$	$-\overset{\|}{C}-$ O	$-CH_2-$	$-CH_3$	X
H	131.56	129.91	128.84	131.49	128.84	129.91	144.56	134.12	43.48	163.65	62.67	13.68	
3-Me	131.36	130.56	138.57	132.32	128.75	127.04	144.64	133.86	43.50	163.79	62.61	13.68	21.27
3-OMe	132.65	114.98	159.80	117.35	129.92	122.31	144.32	134.41	43.50	163.68	62.73	13.70	55.36
3-F	133.52 (J=0.39)	116.28 (J=1.14)	162.64 (J=12.39)	118.36 (J=1.06)	130.54 (J=0.42)	125.89 (J=0.15)	143.01 (J=0.12)	135.58	43.43	163.23	62.90	13.68	
3-Cl	133.49	129.41	134.81	131.26	130.13	128.04	142.94	135.58	43.41	163.16	62.91	13.67	
3-Br	132.22	132.29	122.78	134.16	130.34	128.46	142.82	135.63	43.41	163.16	62.91	13.72	
$3-CF_3$	132.09	126.30 (J=0.20)		127.76 (J=0.18)	129.53	133.06	142.95	136.21	43.43	163.10	63.04	13.60	
3-CN	132.93	133.75	113.46	134.17	129.82	132.84	142.27	136.89	43.39	162.68	63.12	13.74	
$3-NO_2$	133.16	124.12		125.58	130.01	135.60	141.94	137.17	43.39		63.25	13.72	
4-Me	128.54	129.60	130.19	142.42	130.19	129.60	144.59	132.82	43.54	163.84	62.61	13.74	21.57
4-OMe	123.73	132.63	114.40	162.59	114.40	132.63	144.54	130.96	43.67	163.98	62.55	13.83	55.50
$4-NMe_2$	118.25	133.49	111.34	152.75	111.34	133.49	146.01	126.21	43.94	164.46	62.10	13.95	39.97
4-F	127.66 (J=0.18)	132.40 (J=0.44)	116.19 (J=1.11)	164.53 (J=12.72)	116.19 (J=1.11	132.40 (J=0.44)	143.50	133.90	43.51	163.48	62.78	13.74	
4-Cl	129.93	131.25	129.22	137.74	129.22	131.25	143.29	134.65	43.48		62.84	13.73	
4-Br	130.28	131.31	132.14	126.13	132.14	131.31	143.36	134.62	43.42	163.28	62.85	13.73	
$4-NO_2$	137.85	130.53	124.33		124.33	130.53	142.14	137.85	43.34	162.61	63.19	13.74	

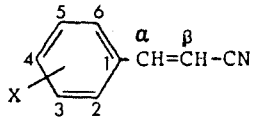
Table R-5

Methyl Styryl Sulphanes



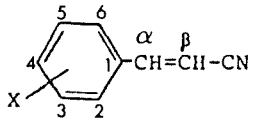
Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	$-CH_3$	X
H	132.19	128.60	129.19	131.40	129.19	128.60	144.00	126.37	43.29	
3-Me	132.16	129.21	138.96	132.21	129.07	125.81	144.15	126.14	43.30	21.26
3-OMe	133.40	113.51	160.06	117.23	130.18	121.19	143.89	126.56	43.26	55.38
3-F	134.38 (J=0.38)	114.89 (J=1.11)	163.02 (J=12.38)	118.30 (J=1.07)	130.85 (J=0.41)	124.68 (J=0.16)	142.53 (J=0.12)	127.87	43.19	
3-Cl	133.98	128.26	135.28	131.26	130.44	126.82	142.35	127.92	43.20	
3-Br	134.22	131.19	123.29	134.15	130.69	127.28	142.20	127.92	43.19	
3-CF_3	133.07	125.11 (J=0.19)		127.76 (J=0.18)	129.87	131.78	142.16	128.51	43.17	
3-CN	132.91	131.77		134.18	130.16	132.54	141.17	129.25	43.09	
3-NO_2	133.95	122.82		125.56	130.37	134.27	141.11	129.67	43.12	
4-Me	129.46	128.62	129.91	142.03	129.91	128.62	143.98	125.19	43.36	21.53
4-OMe	124.77	130.39	114.64	162.25	114.64	130.39	143.63	123.56	43.48	55.45
4-F	128.50 (J=0.18)	130.69 (J=0.44)	116.46 (J=1.11)	164.55 (J=12.66)	116.46 (J=1.11)	130.69 (J=0.44)	142.69	126.19 (J=0.13)	43.32	
4-Cl	130.67	129.77	129.55	137.57	129.55	129.77	142.60	126.94	43.27	
4-Br	131.05	129.93	132.49	125.88	132.49	129.93	142.66	127.00	43.26	

Table R-6

trans-cinnamonitriles 

Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	Other
H	133.54	127.37	124.12	131.21	129.12	127.37	150.54	96.36	
3-Me	133.57	128.00	138.91	132.06	129.02	124.57	150.76	96.10	21.26
3-OMe	134.87	112.56	160.07	116.86	130.19	119.99	150.51	96.72	55.39
3-F		113.78 (J=1.12)		118.16 (J=1.07)	130.83 (J=0.43)	123.45 (J=0.16)	148.19 (J=0.15)	98.04	
3-Cl	134.59	123.17	135.24	131.10	130.41	125.58	148.96	98.09	
3-Br	135.50	130.62	123.27	133.90	130.08	125.99	148.82	98.08	
3-CF_3		124.06 (J=0.18)		127.63 (J=0.20)	129.82	130.38	148.82	98.73	
3-CN	134.08	130.62	113.72	132.52	130.42	131.44	147.94	99.52	
3-NO_2	134.67	122.03		125.44	130.71	133.16	147.82	100.02	
4-Me	130.92	127.35	129.84	141.82	129.84	127.35	150.50	95.09	21.48
4-OMe	126.38	129.11	114.56	162.11	114.56	129.11	150.03	93.38	55.45
4-NMe_2	121.48	129.04	111.72	152.23	111.72	129.04	150.53	89.43	40.04
4-F	130.77 (J=0.20)	129.40 (J=0.44)	116.40 (J=1.10)	164.45 (J=12.65)	116.40 (J=1.10)	129.40 (J=0.44)	149.20 (J=0.04	96.22 (J=0.12)	
4-Cl	132.04	128.56	129.46	137.32	129.46	128.56	149.10	97.07	
4-Br	131.98	128.71	132.41	125.64	132.41	128.71	149.17	97.16	
4-NO_2		128.18	124.41		124.41	128.18	147.81	101.04	

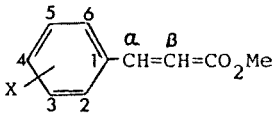
Table R-7

cis-cinnamonitriles 

Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	Other
H		129.12	128.92	130.96	128.92	129.12	148.69	95.08	
3-Me	133.63	129.69	138.68	131.80	128.85	126.15	148.84	94.81	21.31
3-OMe		113.32		117.47	129.97	121.92	148.69	95.30	55.41
3-F		115.65 (J=1.13)		117.96 (J=1.08)	130.61 (J=0.39)	124.87 (J=0.15)	147.30 (J=0.13)	96.72	
3-Cl		129.12		131.10	130.26	126.77	147.08	96.85	
3-Be	135.43	132.06	122.94	133.80	130.48	127.10	146.94	96.87	
3-CF_3					129.68	133.19	147.05	97.51	
3-CN	134.62	132.28		134.71	129.44	133.92	146.14	98.34	
3-NO_2		124.01		125.24	130.27	135.15	146.07	98.80	
4-Me	131.03	129.09	129.62	141.54	129.62	129.09	148.62	93.79	21.53
4-OMe		130.96	114.31	161.69	114.31	130.96	148.06	91.91	55.45
4-NMe_2	119.73	130.94	112.05		112.05	130.94	148.39	87.81	40.04
4-F	129.92 (J=0.24)	131.23 (J=0.44)	116.15 (J=1.12)	164.00 (J=12.66)	116.15 (J=1.12)	131.23 (J=0.44)	147.34	94.76 (J=0.14)	
4-Cl		130.26	129.26		129.26	130.26	147.25	95.75	
4-Br		130.41	132.22		132.22	130.41	147.39	95.89	
4-NO_2		130.36	124.10		124.10	130.36	146.10	99.67	

Table R-8

methyl cinnamates



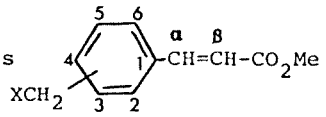
Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	CO	CH_3	Other
H	134.49	128.10	128.92	130.29	128.92	128.10	144.87	117.89	167.39	51.64	
3-Me	134.36	128.79	138.57	131.18	128.79	125.29	145.15	117.57	167.60	51.67	21.30
3-OMe	135.84	113.07	160.00	116.16	129.91	120.79	144.81	118.21	167.32	51.65	55.31
3-OPh	136,23	117,62	156.64	120.50	130.21	122.99	144.18	118.55		51.70	a
3-NMe_2	135.09	111.91		114.54	129.51	116.31	146.04	117.29	167.62	51.61	40.48
3-F	136.72 (J=0.38)	114.35 (J=1.08)		117.17 (J=1.07)	130.47 (J=0.40)	124.09 (J=0.14)	143.48 (J=0.14)	119.31	167.04	51.81	
3-Cl	136.28	127.82	134.98	130.14	130.14	126.23	143.21	119.37	166.94	51.78	
3-Br	136.56	130.77	123.06	133.06	130.37	126.64	143.10	119.39	166.89	51.78	
3-I	136.52	136.71	94.65	138.96	130.46	127.19	143.01	119.14	166.89	51.76	
3-CF_3	135.31	124.67 (J=0.20)		126.72 (J=0.19)	129.52	131.09	143.07	119.92	166.91	51.89	
3-CN	135.73	131.34	113.48	133.23	129.86	131.91	142.07	120.64	166.63	51.99	
3-NO_2	136.23	127.46		124.55	130.02	133.61	141.96	121.08	166.54	51.98	
4-Me	131.76	128.09	129.63	140.69	129.63	128.09	144.87	116.76	167.60	51.58	21.44
4-OMe	127.21	129.73	114.36	161.44	114.36	129.73	144.52	115.35	167.72	51.52	55.35
4-OPh	129.23	129.76	118.44		118.44	129.76	144.14	116.53	167.56	51.64	b
4-NMe_2	122.31	129.73	111.87	151.82	111.87	129.73	145.35	112.30		51.31	40.09
4-F	130.18 (J=0.15)	129.97 (J=0.41)	116.08 (J=1.09)	163.99 (J=12.57)	116.08 (J=1.09)	129.97 (J=0.41)	143.55	117.68 (J=0.12)		51.68	
4-Cl		129.25	129.25		129.25	129.25	143.26	118.48		51.78	
4-Br	133.30	129.44	132.14	124.52	132.14	129.44	132.46	118.51	167.09	51.76	
4-I	133.84	129.49	138.08	96.49	138.08	129.49	143.59	118.55	167.09	51.76	
4-CN		128.38	132.62		132.62	128.38	142.39	121.41		52.03	
4-NO_2	140.71	128.66	124.21	151.01	124.21	128.66	141.88	122.40	166.39	51.95	

a The chemical shifts assigned to the phenoxy ring carbons are: 157.94 ($C_{1'}$); 119.21 ($C_{2'}$, $C_{6'}$); 129.92 ($C_{3'}$,$C_{5'}$); 123.77 ($C_{4'}$).

b The chemical shifts assigned to the phenoxy ring carbons are: 118.44 ($C_{2'}$,$C_{6'}$); 129.96 ($C_{3'}$,$C_{5'}$); 124.14 ($C_{4'}$).

Table R-9

methyl (substituted methyl) cinnamates



CH_2X	C_1	C_2	C_3	C_4	C_5	C_6	C_α	C_β	CO	CH_3	$-CH_2-$	Other
3-CH_3	134.36	128.79	138.57	131.18	128.79	125.29	145.15	117.57	167.60	51.67	21.30	
3-CH_2CH_3	134.46	127.62		130.02	128.89	125.53	145.19	117.57		51.65	28.75	15.47
3-CH_2OMe		127.39		129.48	128.95	127.10	144.70	118.08		51.66	74.25	58.25
3-CH_2OPh	134.80	126.94	138.03	129.17	129.56	127.58	144.52	118.28	167.31	51.70	69.47	a
3-CH_2NMe_2	134.60	128.82		131.20	128.94	127.17	144.75	118.06		51.66		45.09
3-CH_2F	134.84	126.73 (J=0.34)	137.69 (J=0.39)	129.02 (J=0.35)	129.19	128.29 (J=0.14)	144.19	118.55	167.23	51.74	84.03 (J=4.20)	
3-CH_2Cl	135.01	128.07	138.27	129.34	128.47	127.97	144.13	118.60		51.75	45.65	
3-CH_2Br	135.06	128.52	138.63	130.76	129.39	127.98	144.04	118.65	167.19	51.73	32.66	
3-CH_2I		128.25		130.53	129.42	127.46	144.10	118.56		51.74	4.38	
3-CH_2CN		127.71		129.78	129.61	127.42	143.70	119.10		51.79	23.51	
3-CH_2NO_2	135.78	129.69	138.71	131.55	129.77	129.50	143.50	119.34		51.85	79.67	
4-CH_3	131.76	128.09	129.63	140.69	129.63	128.09	144.87	116.76	167.60	51.58	21.44	
4-CH_2CH_3		128.16	128.42		128.42	128.16	144.90	116.75		51.60	28.77	15.28
4-CH_2OMe		128.00	128.14		128.14	128.00	144.54	117.75		51.66	74.19	58.28
4-CH_2OPh	134.01	128.31	127.76	139.53	127.76	128.31	144.47	117.92	167.51	51.75	69.41	b
4-CH_2NMe_2	133.37	128.10	129.62		129.62	128.10	144.66	117.51		51.64	63.94	45.30
4-CH_2F		128.25	127.63 (J=0.31)		127.63 (J=0.31)	128.25	144.09	118.45 (J=0.06)		51.75	83.93 (J=4.20)	
4-CH_2Cl	134.55	128.40	129.12	139.54	129.12	128.40	143.98	118.53		51.74	45.59	
4-CH_2Br		128.46	129.58		129.58	128.46	143.94	118.51		51.72	32.62	
4-CH_2CN		128.71	128.51		128.51	128.71	143.65	118.75		51.76	23.53	
4-CH_2NO_2	136.05	128.57	130.53		130.53	128.57	143.41	119.46	167.01	51.67	79.48	

a The chemical shifts assigned to the phenoxy ring carbons are: 158.57 ($C_{1'}$); 114.87 ($C_{2'}$,$C_{6'}$); 129.56 ($C_{3'}$,$C_{5'}$); 121.17 ($C_{4'}$).

b The chemical shifts assigned to the phenoxy ring carbons are: 158.57 ($C_{1'}$); 114.87 ($C_{2'}$,$C_{6'}$); 129.55 ($C_{3'}$,$C_{5'}$); 121.17 ($C_{4'}$).

Table R-10 ^{13}C NMR Substituent Chemical Shifts[a] for the β Sidechain Carbon in a Series of β-Carbomethoxystyrenes in Six Solvents.

Substituent	$(CH_3)_2CO$	$(CH_3)_2CO$	C_2H_5OH	$CDCl_3$	CCl_4	C_6H_6
H	118.73	117.76	118.22	117.89	117.91	118.41
3-Me	-0.25	-0.25	-0.27	-0.28	-0.25	-0.23
3-OMe	0.27	0.33	0.19	0.32	0.14	0.20
3-OPh	0.99	0.92	0.88	0.96	0.93	0.76
$3-NMe_2$	-0.76	-0.70	-0.83	-0.60	-0.71	-0.58
3-F	1.63	1.62	1.65	1.39	1.41	1.31
3-Cl	1.76	1.70	1.71	1.47	1.47	1.31
3-Br	1.76	1.68	1.72	1.49	1.49	1.30
3-I	1.46	1.38	1.52	1.29	1.33	1.16
$3-CF_3$	2.28	2.20	2.30	2.01	2.01	1.74
3-CN	2.60	2.55	2.91	2.73	2.63	2.12
$3-NO_2$	3.02	3.00	3.36	3.20	3.08	2.53
$3-CH_2CH_3$	-0.25	-0.18	-0.30	-0.31	-0.29	-0.22
$3-CH_2OCH_3$	0.10	0.17	0.24	0.18	0.07	0.11
$3-CH_2OPh$	0.39	0.42	0.35	0.40	0.35	0.37
$3-CH_2NMe_2$	0.29	0.23	0.30	0.18	-0.10	0.07
$3-CH_2F$	0.57	0.58	0.68	0.67	0.65	0.54
$3-CH_2Cl$	0.68	0.63	0.68	0.74	0.72	0.59
$3-CH_2Br$	0.69	0.62	0.69	0.79	0.79	0.59
$3-CH_2I$	0.63	0.49	0.56	0.68	0.67	0.52
$3-CH_2CN$	0.88	0.79	1.00	1.22	1.17	0.90
$3-CH_2NO_2$	1.01	0.84	1.22	1.44	1.40	1.05
4-Me	-1.19	-1.09	-1.13	-1.10	-1.04	-0.99
$4-CH_2CH_3$	-1.17	-1.07	-1.08	-1.10	-1.01	-0.95
$4-CH_2OCH_3$	-0.26	-0.25	-0.14	-0.13	-0.27	-0.24
$4-CH_2OPh$	0.04	0.05	0.00	0.03	-0.01	0.03
$4-CH_2NMe_2$	-0.35	-0.33	-0.08	-0.37	-0.52	-0.41
$4-CH_2F$	0.52	0.57	0.54	0.56	0.53	0.46
$4-CH_2Cl$	0.58	0.58	0.55	0.65	0.61	0.48
$4-CH_2Br$	0.53	0.54	0.59	0.66	0.64	0.53
$4-CH_2CN$	0.52	0.40	0.64	0.86	0.81	0.58
$4-CH_2NO_2$	1.24	1.17	1.44	1.61	1.51	1.27

[a] The spectra were referenced to tetramethylsilane as an internal standard and the $^{13}C_\beta$ chemical shifts for the substituted methyl cinnamates are quoted here as differences from the unsubstituted compound.

Table R-11 ^{13}C NMR Substituent Chemical Shifts[a] for the α- Sidechain Carbon in a Series of β-Carbomethoxystyrenes in Six Solvents

Substituent	Solvent					
	$(CH_3)_2CO$	$(CH_3)_2SO$	C_2H_5OH	$CDCl_3$	CCl_4	C_6H_6
H	145.24	144.47	145.85	144.89	144.02	144.77
3-Me	0.15	0.10	0.23	0.19	0.24	0.29
3-OMe	-0.01	-0.06	-0.01	-0.14	0.09	0.11
3-OPh	-0.78	-0.82	-0.77	-0.72	-0.59	-0.76
$3-NMe_2$	1.34	1.21	1.33	1.14	1.33	1.48
3-F	-1.43	-1.46	-1.55	-1.38	-1.38	-1.45
3-Cl	-1.74	-1.67	-1.86	-1.70	-1.68	-1.79
3-Br	-1.75	-1.71	-1.86	-1.80	-1.63	-1.80
3-I	-1.77	-1.67	-1.89	-1.85	-1.75	-1.82
$3-CF_3$	-1.76	-1.77	-1.95	-1.85	-1.78	-1.96
3-CN	-2.37	-2.29	-2.72	-2.85	-2.59	-2.74
$3-NO_2$	-2.50	-2.44	-2.77	-2.93	-2.70	-2.88
$3-CH_2CH_3$	0.25	0.29	0.25	0.30	0.31	0.44
$3-CH_2OMe$	-0.04	-0.11	-0.16	-0.19	0.00	-0.03
$3-CH_2OPh$	-0.19	-0.20	-0.22	-0.37	-0.23	-0.26
$3-CH_2NMe_2$	-0.16	-0.15	-0.23	-0.14	0.16	0.19
$3-CH_2F$	-0.45	-0.55	-0.53	-0.70	-0.58	-0.55
$3-CH_2Cl$	-0.63	-0.59	-0.65	-0.74	-0.72	-0.67
$3-CH_2Br$	-0.70	-0.64	-0.72	-0.83	-0.74	-0.79
$3-CH_2I$	-0.64	-0.59	-0.58	-0.79	-0.66	-0.73
$3-CH_2CN$	-0.78	-0.69	-0.90	-1.19	-1.02	-1.00
$3-CH_2NO_2$	-0.88	-0.92	-1.02	-1.41	-1.27	-1.24
4-Me	-0.01	0.03	0.06	0.01	-0.04	0.05
$4-CH_2CH_3$	0.09	-0.01	0.10	0.04	0.00	0.10
$4-CH_2OMe$	-0.20	-0.30	-0.36	-0.35	-0.21	-0.21
$4-CH_2OPh$	-0.37	-0.36	-0.23	-0.43	-0.33	-0.41
$4-CH_2NMe_2$	-0.22	-0.24	-0.41	-0.23	-0.12	-0.10
$4-CH_2F$	-0.60	-0.62	-0.66	-0.81	-0.76	-0.73
$4-CH_2Cl$	-0.72	-0.64	-0.78	-0.91	-0.79	-0.78
$4-CH_2Br$	-0.79	-0.73	-0.83	-0.92	-0.89	-0.84
$4-CH_2CN$	-0.79	-0.73	-0.96	-1.25	-1.16	-1.09
$4-CH_2NO_2$	-1.00	-0.92	-1.13	-1.45	-1.24	-1.24

[a] The $^{13}C_\alpha$ NMR chemical shifts for the substituted methyl cinnamates are quoted here as differences from the chemical shifts of the unsubstituted compound.

Table R-12 ^{19}F NMR Chemical Shifts, in ppm from external trifluoroacetic acid, for 3-fluorobenzyl derivatives in five solvents.

Substituent	$(CH_3)_2CO$	$(CH_3)_2SO$	$CHCl_3$	CCl_4	C_6H_6
H	-38.60	-36.37	-36.51	-35.41	-36.90
CH_3	-38.40	-36.13	-36.27	-35.13	-36.64
OCH_3	-37.95	-35.69	-35.49	-34.65	-36.12
OC_6H_5	-37.58	-35.39	-35.03	-34.04	-35.70
$N(CH_3)_2$	-38.30	-35.98	-35.66	-35.07	-36.57
F	-37.42	-35.08	-34.89	-33.85	-35.60
Cl	-37.30	-35.15	-34.72	-33.76	-35.50
Br	-37.30	-35.15	-34.65	-33.68	-35.41
I	-37.27	-35.19	-34.62	-33.64	-35.43
CN	-36.84	-34.78	-33.83	-32.89	-34.92
NO_2	-37.02	-35.04	-33.73	-32.73	-34.82

Table R-13 ^{19}F NMR chemical shifts, in ppm from external trifluoroacetic acid, for 4-fluorobenzyl derivatives in five solvents.

Substituent	$(CH_3)_2CO$	$(CH_3)_2SO$	$CHCl_3$	CCl_4	C_6H_6
H	-42.93	-40.62	-40.86	-39.60	-41.16
CH_3	-42.60	-40.18	-40.49	-39.17	-40.79
OCH_3	-39.82	-37.45	-37.12	-36.55	-38.05
OC_6H_5	-39.17	-36.76	-36.55	-35.74	-37.33
$N(CH_3)_2$	-40.39	-38.20	-37.77	-37.31	-38.67
F	-37.61	-35.27	-35.06	-34.36	-35.99
Cl	-37.95	-35.76	-35.50	-34.63	-36.36
Br	-37.80	-35.52	-35.17	-34.29	-36.07
I	-38.23	-36.21	-35.64	-34.74	-36.49
CN	-39.21	-37.11	-36.10	-35.25	-37.29
NO_2	-36.17	-34.13	-32.72	-31.97	-34.12

DISCUSSION

General

The discussion of the results presented in this thesis is divided into three sections. The first section consists of a qualitative comparison among the various systems chosen for investigation and considers the extent to which some of the chemical shifts reflect the inductive effect of substituents. The second section considers the effect of solvent on the inductive substituent constant, σ_I. It concludes by calculating values for σ_I and σ^{meta} for a number of substituents in the various solvents used. In the final part the effect of changing the β-substituent in series of β-substituted styrenes on the ^{13}C NMR chemical shifts of the α- and β-carbons is interpreted.

In referring to side-chain carbons in methylcinnamates, and in particular in comparing them to similar carbons of styrene derivatives, there is a problem regarding nomenclature. It is generally accepted that if we speak of the α-carbon of a styrene then we are referring to that ethenyl carbon directly linked to the aromatic nucleus, and that the β-carbon is the more distant one. In contrast, in compounds such as the cinnamic acids and their derivatives the acid moiety takes priority and the term α-carbon must be taken to apply to that carbon of the ethenyl group that is directly linked to carboxyl function. The result is that C_α of a styrene is C_β of a methyl cinnamate, and vice-versa. A similar situation is also encountered in some other series. In order

to avoid confusion in the discussion that follows, compounds will often be named and discussed as derivatives of styrene rather than their more commonly used alternatives, thus, for example, the methyl cinnamates become the β-carbomethoxystyrenes, and the cinnamonitriles the β-cyanostyrenes.

1. THE SYSTEMS CHOSEN FOR INVESTIGATION OF THE INDUCTIVE EFFECT

This section is further subdivided into three parts. The first part looks at the ^{13}C NMR substituent chemical shifts (SCS's) for the β-carbon of various β-substituted styrenes. The second looks at the $^{13}C_{\alpha}$ SCS's of the same systems, while in the third part the ability of ^{19}F NMR SCS's to reflect the inductive effect of substituents is considered.

1.1 $^{13}C_{\beta}$ NMR Substituent Chemical Shifts

1.1.1 The X-substituted β-Carbomethoxystyrenes

Happer has shown that the ^{13}C NMR chemical shifts of the β-carbon in β-substituted styrenes show an excellent correlation with σ^{meta} values when the ring is substituted in the meta-position.[22] Table D-1 lists the ^{13}C SCS's obtained in this study for the β-carbon in a series of meta-substituted β-carbomethoxystyrenes (I).

(I)

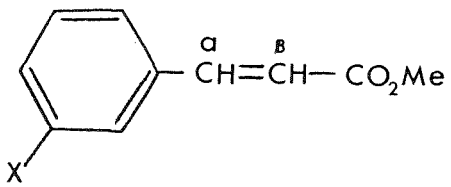


TABLE D-1

Substituent Chemical Shifts[a] for $^{13}C_{\beta}$ of X- Ring Substituted-β-carbomethoxystyrenes

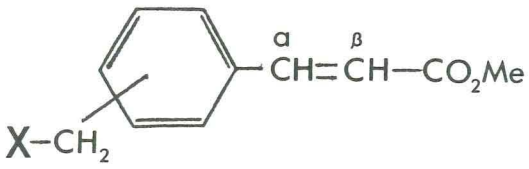
Substitutent	SCS (C_{β}) in EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
H	0.00	0.00	0.00	0.00	0.00	0.00
3-CH_3	-0.27	-0.25	-0.25	-0.28	-0.25	-0.23
3-$N(CH_3)_2$	-0.83	-0.70	-0.76	-0.60	-0.71	-0.58
3-OCH_3	0.19	0.33	0.27	0.32	0.14	0.20
3-OC_6H_5	0.88	0.92	0.99	0.96	0.93	0.76
3-F	1.65	1.62	1.63	1.39	1.41	1.31
3-Cl	1.71	1.70	1.76	1.47	1.47	1.31
3-Br	1.72	1.68	1.76	1.49	1.49	1.30
3-I	1.52	1.38	1.46	1.29	1.33	1.16
3-CF_3	2.30	2.20	2.28	2.01	2.01	1.74
3-CN	2.91	2.55	2.60	2.73	2.63	2.12
3-NO_2	3.36	3.00	3.02	3.20	3.08	2.53
4-CH_3	-1.13	-1.09	-1.19	-1.10	-1.04	-0.99

[a] These chemical shifts are expressed as differences from the unsubstituted shift of the β-carbomethoxystyrene in the solvent concerned.

The only point to note at this stage is that these SCS values give an excellent correlation with those obtained by Happer[21] for C_β of styrenes in the same solvent (SD/RMS=0.03 for all) Thus these $^{13}C_\beta$ SCS values should, like those of the styrenes, give good correlations with Hammett σ^{meta} values.

1.1.2 The XCH_2-substituted β-carbomethoxystyrenes.

It is commonly accepted that the interposition of a methylene ($-CH_2-$) group between a substituent and an aromatic system has the effect of eliminating all direct resonance interaction between the substituent and the aromatic system while still allowing the inductive effect to retain its influence, although its magnitude is significantly reduced. With this in mind, the ^{13}C NMR SCS values for the β-carbon in series of meta- and para- XCH_2-substituted β-carbomethoxystyrenes (II) were studied. These SCS values, recorded in six solvents, are listed in Table D-2.



(II)

Since the data in Table D-1 can be correlated by the Hammett equation, then the data for both the meta-XCH_2

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TABLE D-2

Substitutent Chemical Shifts for $^{13}C_{\beta}$ in XCH_2- Ring

Substituted β-Carbomethoxystyrenes

	SCS (C_{β}) in					
Substituent	EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
H	0.00	0.00	0.00	0.00	0.00	0.00
3-CH_3	-0.27	-0.25	-0.25	-0.28	-0.25	-0.23
3-CH_3CH_2	-0.30	-0.18	-0.25	-0.31	-0.29	-0.22
3-CH_3OCH_2	0.24	0.17	0.10	0.18	0.07	0.11
3-$C_6H_5OCH_2$	0.35	0.42	0.39	0.40	0.35	0.37
3$(CH_3)_2NCH_2$	0.30	0.23	0.29	0.18	-0.10	0.07
3-FCH_2	0.68	0.58	0.57	0.67	0.65	0.54
3-$ClCH_2$	0.68	0.63	0.68	0.74	0.72	0.59
3-$BrCH_2$	0.69	0.62	0.69	0.79	0.79	0.59
3-ICH_2	0.56	0.49	0.63	0.68	0.67	0.52
3-$NCCH_2$	1.00	0.79	0.88	1.22	1.17	0.90
3-O_2NCH_2	1.22	0.84	1.01	1.44	1.40	1.05
4-CH_3	-1.13	-1.09	-1.19	-1.10	-1.04	-0.99
4-CH_3CH_2	-1.08	-1.07	-1.17	-1.10	-1.01	-0.95
4-CH_3OCH_2	-0.14	-0.25	-0.26	-0.13	-0.27	-0.24
4-$C_6H_5OCH_2$	0.00	0.05	0.04	0.03	-0.01	0.03
4-$(CH_3)_2NCH_2$	-0.08	-0.33	-0.35	-0.37	-0.52	-0.41
4-FCH_2	0.54	0.57	0.52	0.56	0.53	0.46
4-$ClCH_2$	0.55	0.58	0.58	0.65	0.61	0.48
4-$BrCH_2$	0.59	0.54	0.53	0.66	0.64	0.53
4-$NCCH_2$	0.64	0.40	0.52	0.86	0.81	0.58
4-O_2NCH_2	1.44	1.17	1.24	1.61	1.51	1.27

and para- XCH_2 series, in the same solvent, might be expected to correlate well not only with each other, but also with σ_I. Three graphs are shown in Figure 1(a) - 1(c). These are plots of SCS (m-XCH_2-) v. SCS (p-XCH_2-), SCS (m-XCH_2-) v. σ_I, and SCS (p-XCH_2-) v. σ_I respectively. Ethanol was the solvent in each case.

From these graphs it is evident that a few complications have arisen, in that a number of the SCS values seem anomalous. In Figure 1(a) the correlation is excellent for all points except $NCCH_2$-. Consideration of 1(b) and 1(c) suggests that it is the shift for the p-$NCCH_2$ derivative that is responsible for the anomaly, its $^{13}C_\beta$ SCS lying about 0.5 ppm upfield from its expected position. The shifts for this substituent recorded in the other solvents (see next section) verify that this anomaly is real and not just experimental error. Similar behaviour for this substituent is observed in the ^{19}F NMR substituent chemical shifts in the p-XCH_2-fluorobenzenes (Table D-9).

From consideration of Figures 1(b) and 1(c) it becomes apparent that the correlations of the meta- and para- XCH_2 SCS data sets with σ_I are much less satisfactory than their correlation with one another. It would appear that either σ_I's have different values in ethanol from those in aqueous solution or at least some SCS's are being influenced by some property or properties other than the inductive effect of the substituents. One case which clearly falls into the first category is the $MeOCH_2$- substituent. The $^{13}C_\beta$ data for both the meta- X- substituted β-carbomethoxystyrenes

and the meta- X- substituted styrenes (reproduced in Table D-3 from Happer's study[21] of this series) suggest that σ_I for the -OMe group in ethanol is lower than in aqueous solution by at least 0.05 σ_I units. Allowing for this solvent effect brings the methoxy substituent into line. Taft and co-workers[14] also noted a solvent dependence of σ_I for the methoxy substituent. A similar explanation can be offered for the observed shift of the phenoxy substituent but the discrepancy may be a little high to account for entirely in this way.

The dimethylamino group appears to be substantially more electron withdrawing than we would normally expect for this group. It is possible that this is due to an interaction with the ethanol solvent or even with carbon dioxide (it is strongly basic) and it is certainly not impossible that some property other than the inductive effect may be influencing the SCS's for this substituent.

Fluorine (σ_I = 0.54) is usually considered to be significantly more inductively electron withdrawing than either of the chloro or bromo substituents (σ_I = 0.47), but it can be seen from Table D-2 that in all cases the SCS for FCH_2- is the same as,or less than, that for $ClCH_2$- or $BrCH_2$. The literature σ_I value for the fluoro substituent has not been widely studied. Charton[47] has presented an extensive compilation of reactions that can be used to determine σ_I data and amongst these reactions only eight series include the fluoro substituent. Of the eight, four are the ionisation of acetic acids in water at various

Table D-3

Positions of C_β resonances in meta- and para- substituted styrenes

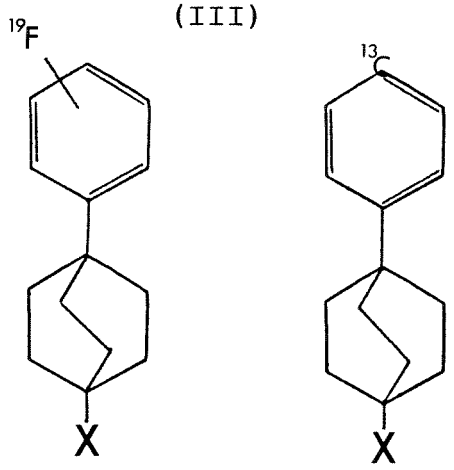
All resonance positions are expressed in ppm upfield or downfield relative to C_β for styrene. Relative to $SiMe_4$ the styrene values are: 75% EtOH-D_2O, 113.83; EtOH, 113.62; Me_2SO, 114.10; Me_2CO; 113.99; $CDCl_3$, 113.76; CCl_4, 113.20; C_6H_6, 113.61.

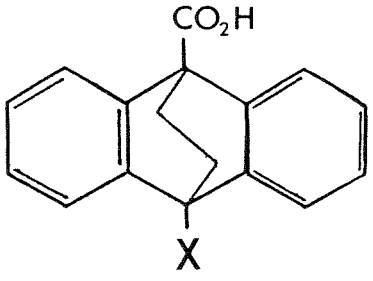
ring substituent	solvent						
	75%EtOH	EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
H	0.00	0.00	0.00	0.00	0.00	0.00	0.00
m-Me	-0.18	-0.24	-0.23	-0.26	-0.20	-0.26	-0.22
p-Me	-1.05	-1.03	-1.13	-1.08	-1.01	-1.00	-1.04
m-OMe	0.46	0.22	0.31	0.24	0.28	0.19	0.24
p-OMe	-2.14	-2.31	-2.48	-2.44	-2.20	-2.22	-2.24
m-F	1.72	1.65	1.76	1.73	1.40	1.42	1.37
p-F	0.01	-0.11	-0.11	-0.04	-0.26	-0.19	-0.33
m-Cl	1.89	1.82	1.93	1.90	1.55	1.55	1.55
p-Cl	1.09	0.97	1.00	1.02	0.68	0.77	0.64
m-Br	1.97	1.90	1.91	1.95	1.61	1.67	1.51
p-Br	1.21	1.09	1.07	1.05	0.78	0.90	0.69
m-CF_3	2.48	2.39	2.40	2.45	2.04	2.19	1.97
p-CF_3	3.31	3.13	3.23	3.09	2.73	2.82	2.60
m-CN	3.28	3.16	2.92	2.92	2.84	2.99	2.46
p-CN	4.57	4.24	4.19	4.05	3.92	3.85	3.37
m-NO_2	3.69	3.56	3.41	3.50	3.31	3.32	2.87
p-NO_2	5.43	5.11	5.22	5.08	4.79	4.56	4.18

temperatures and of the other four, three favour the inductive order F < Cl,Br. However the observed differences amongst these halogens are quite small. Tafts ^{19}F SCS data for the <u>meta</u>-substituted fluorobenzenes[14] give the order of F > Br but ^{13}C and ^{19}F chemical shift measurements by Adcock and Khor[16h] on 1-X-4-phenylbicyclo-[2,2,2]-octanes(III) support F < Cl,Br.

Stock and co-workers[83] report dissociation constants of 4-substituted dibenzobicyclo-[2,2,2]-octa-2,5 diene carboxylic acids (IV) which also give the order observed by Adcock and Khor s that it seems that we may not be dealing with a specific NMR phenomenon but that σ_I for the fluoro substituent might vary according to the mechanism by which the effect is transmitted.

(III)





(IV)

Unfortunately no adequate explanation can be offered for the observed substantial upfield shift for the para-$NCCH_2$- substituent. The fact that the deviation is very small in the case of the meta-$NCCH_2$- compound compared with this substituent in the para-position suggests that enhancement of the hyperconjugative effect of this group may be involved. However, no similar effect is observed for the O_2NCH_2- substituent and the nitro group should influence the resonance ability of the methylene group in much the same way as the cyano group. No anomaly is found for the cyano substituent in either Exner's study[43] of the pK_a's of 4-XCH_2- substituent benzoic acids or Fischer's study[44] of the pK_a's of 4-XCH_2- substituted pyridinium ions, although it must be noted that for both of these latter systems the extent of +R type resonance interaction would be expected to be significantly lower than in the methyl cinnamates.

In their investigations, both Exner and Fischer noted that a plot of the data for the para-XCH_2- compounds against the data for the meta-XCH_2-compounds gave lines for which the slopes were close to unity (1.14 and 0.95 respectively). The slope in Figure 1(a) has a value of about 1.8 . Note that this slope reflects the relative efficiencies of transmission from the meta- and para-positions of the effect of the substituent, $-CH_2X$. The order observed for the three systems is that predicted on the basis of the relative importance in each of the +R interactions between the substituent and the reaction site (the degree of the +R resonance interaction can be

estimated from the observed substituent effect of the para-CH_3- substituent in each case).

Since the inductive effect of the substituent-X- can, in some cases, be transmitted through an interposed methylene group almost twice as efficiently when the XCH_2- group is in the para- rather than the meta- position, it is a little misleading to talk about the "attenuating effect" of the $-CH_2-$ linkage. The implication is that the inductive effect of -X is being relayed to a considerable extent through its effect on the hyperconjugative interaction between the $-CH_2-$ group and the ring. In the para- position such hyperconjugative interaction will be more important than in the meta- position.

In summary, we can say that although the ^{13}C NMR substituent chemical shifts of the β- carbon in the XCH_2-β-carbomethoxystyrenes clearly reflect, for the most part, the inductive effect of the group "X", there are other properties of this system which, for at least some of the substituents, influence these chemical shifts. This makes the system somewhat less useful for our purposes than we would have hoped.

1.2 $^{13}C_\alpha$ NMR CHEMICAL SHIFTS

The effect of meta- and para- substituents on the ^{13}C NMR chemical shifts for the α- carbon of π systems attached to the aromatic ring has been examined by Brownlee and co-workers.[20] In most cases studied, the π system involved was a carbonyl group but the corresponding data for styrene

derivatives show similar trends. Brownlee observed that the $^{13}C_{\alpha}$ SCS's followed an order which was the reverse to that which would have been expected on the basis of normal substituent effects and the reserse to that observed for the $^{13}C_{\beta}$ SCS's. Thus electron withdrawing substituents produced chemical shifts which were <u>upfield</u> from the shift of the α-carbon in the unsubstituted molecule. This implies <u>increased</u> shielding of the resonating nucleus in the substituted molecule. A more important observation, from the point of view of this thesis, is that these "reversed substituent effects" tend to be dominated by the inductive effect of the substituents. This last conclusion was based on DSP analyses of the $^{13}C_{\alpha}$ data. The explanation of Brownlee for these observations involved the postulation of a localized polarization of the side-chain π system by a through space field effect. However, the DSP correlations achieved were less than satisfactory and their explanation fails to account for the <u>downfield</u> shifts observed for the strong +R substituents, $-NMe_2$ and $-NH_2$. These latter shifts imply that some kind of reversed resonance effect is also operating.

However, since a wealth of $^{13}C_{\alpha}$ NMR data was available as a by-product from the investigation of ^{13}C chemical shifts of the β-carbon in our study it seemed only prudent to make use of it if possible. The $^{13}C_{\alpha}$ SCS's for the <u>meta</u>-X- substituted β-carbomethoxystyrenes are contained in Table D-4 and the corresponding data for the <u>meta</u>- and <u>para</u>- XCH_2-analogues are in Table D-5. Similar $^{13}C_{\alpha}$ data available

TABLE D-4

Substituent Chemical Shifts for $^{13}C_{\alpha}$ in X- Ring Substituted β-Carbomethoxystyrenes

Substituent	SCS (C_{α}) in EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
H	0.00	0.00	0.00	0.00	0.00	0.00
3-CH_3	0.23	0.10	0.15	0.19	0.24	0.29
3-$N(CH_3)_2$	1.33	1.21	1.34	1.14	1.33	1.48
3-OCH_3	-0.01	-0.06	-0.01	-0.14	0.09	0.11
3-OC_6H_5	-0.77	-0.82	-0.78	-0.72	-0.59	-0.76
3-F	-1.55	-1.46	-1.43	-1.38	-1.38	-1.45
3-Cl	-1.86	-1.67	-1.74	-1.70	-1.68	-1.79
3-Br	-1.86	-1.71	-1.75	-1.80	-1.63	-1.80
3-I	-1.89	-1.67	-1.77	-1.85	-1.75	-1.82
3-CF_3	-1.95	-1.77	-1.76	-1.85	-1.78	-1.96
3-CN	-2.72	-2.29	-2.37	-2.85	-2.59	-2.74
3-NO_2	-2.77	-2.44	-2.50	-2.93	-2.70	-2.88

TABLE D-5

Substituent Chemical Shifts for $^{13}C_{\alpha}$ in XCH_2- Ring Substituted β-Carbomethoxystyrenes

Substituent	SCS (C_α) in EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
H	0.00	0.00	0.00	0.00	0.00	0.00
3-CH_3	0.23	0.10	0.15	0.19	0.24	0.29
3-CH_3CH_2	0.25	0.29	0.25	0.30	0.31	0.44
3-CH_3OCH_2	-0.16	-0.11	-0.04	-0.19	0.00	-0.03
3-$C_6H_5OCH_2$	-0.22	-0.20	-0.19	-0.37	-0.23	-0.26
3-$(CH_3)_2NCH_2$	-0.23	-0.15	-0.16	-0.14	0.16	0.19
3-FCH_2	-0.53	-0.55	-0.45	-0.70	-0.58	-0.55
3-$ClCH_2$	-0.65	-0.59	-0.63	-0.74	-0.72	-0.67
3-$BrCH_2$	-0.72	-0.64	-0.70	-0.83	-0.74	-0.79
3-ICH_2	-0.58	-0.59	-0.64	-0.79	-0.66	-0.73
3-$NCCH_2$	-0.90	-0.69	-0.78	-1.19	-1.02	-1.00
3-O_2NCH_2	-1.02	-0.92	-0.88	-1.41	-1.27	-1.24
4-CH_3	0.06	0.03	-0.01	0.01	-0.04	0.05
4-CH_3CH_2	0.10	-0.01	0.09	0.04	0.00	0.10
4-CH_3OCH_2	-0.36	-0.30	-0.20	-0.35	-0.21	-0.21
4-$C_6H_5OCH_2$	-0.23	-0.36	-0.37	-0.43	-0.33	-0.41
4-$(CH_3)_2NCH_2$	-0.41	-0.24	-0.22	-0.23	-0.12	-0.10
4-FCH_2	-0.66	-0.62	-0.60	-0.81	-0.76	-0.73
4-$ClCH_2$	-0.78	-0.64	-0.72	-0.91	-0.79	-0.78
4-$BrCH_2$	-0.83	-0.73	-0.79	-0.92	-0.89	-0.84
4-$NCCH_2$	-0.96	-0.73	-0.79	-1.25	-1.16	-1.09
4-O_2NCH_2	-1.13	-0.92	-1.00	-1.45	-1.24	-1.24

from Happer's study[21] of meta- and para- X- substituted styrenes are listed in Table D-6.

DSP analyses of the data from Tables D-4 - D-6 were performed using Ehrenson, Brownlee and Taft's σ_I and σ_R values. The results are summarized in Table D-7.

The analyses for the X-substituted styrenes and β-carbomethoxystyrenes show similar trends to those observed by Brownlee and co-workers for $^{13}C_\alpha$ SCS's in other side-chains. The success of the correlation, as indicated by the "f" values, is poor here also. The agreement between theory and experiment is considerably less than that expected on the basis of normal measurement errors. This is illustrated in Table D-8 by a comparison between experimental $^{13}C_\alpha$ SCS's and those calculated from the DSP equation for the meta-X- substituted β-carbomethoxystyrenes.

The DSP analyses for the meta- and para-XCH_2- substituted β-carbomethoxstyrenes indicate that these series are more strongly dominated by inductive effects than the X-series since λ (= ρ_R/ρ_I) is close to zero. However the correlations are so poor as to be almost meaningless. These latter $^{13}C_\alpha$ SCS's would be expected to correlate with σ_I with more precision than the $^{13}C_\alpha$ shifts of the X-substituted β-carbomethoxystyrenes since any resonance effects should be very small. Also, as the substituent is one atom further away from C_α, any proximity effects making contributions to the SCS in the X-series should be reduced in the XCH_2-series.

It may be recalled that the $^{13}C_\beta$ SCS data recorded in ethanol for the meta- and para-XCH_2- substituted

TABLE D-6

Substituent Chemical Shifts for $^{13}C_{\alpha}$ in X- Ring Substituted Styrenes

Substituent	SCS (C_{α}) in 75% EtOH	EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
H	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-CH_3	0.11	0.11	0.09	0.07	0.06	0.05	0.13
3-OCH_3	-0.08	-0.05	-0.14	-0.01	-0.07	-0.08	-0.02
3-F	-1.18	-1.12	-1.12	-1.13	-1.09	-1.18	-1.32
3-Cl	-1.35	-1.36	-1.37	-1.42	-1.30	-1.37	-1.58
3-Br	-1.45	-1.44	-1.47	-1.47	-1.40	-1.46	-1.65
3-CF_3	-1.42	-1.40	-1.40	-1.43	-1.23	-1.47	-1.68
3-CN	-2.14	-2.14	-2.00	-2.01	-2.05	-2.13	-2.37
3-NO_2	-2.16	-2.11	-1.95	-1.99	-2.16	-2.12	-2.50
4-CH_3	-0.13	-0.18	-0.18	-0.15	-0.20	-0.23	-0.12
4-OCH_3	-0.61	-0.69	-0.55	-0.59	-0.67	-0.67	-0.56
4-F	-1.22	-1.17	-1.23	-1.25	-1.20	-1.31	-1.36
4-Cl	-1.31	-1.31	-1.27	-1.30	-1.22	-1.27	-1.40
4-Br	-1.26	-1.26	-1.27	-1.23	-1.14	-1.20	-1.34
4-CF_3	-1.40	-1.41	-1.31	-1.43	-1.29	-1.32	-1.57
4-CN	-1.56	-1.59	-1.62	-1.47	-1.51	-1.57	-1.78
4-NO_2	-1.98	-1.89	-1.75	-1.82	-1.92	-1.93	-2.23

TABLE D-7

Summary of the Results from DSP Analyses of the $^{13}C_{\alpha}$ SCS's of the XCH_2- Substituted β-Carbomethoxystyrenes and the X- Substituted Styrenes

Series	ρ_I	ρ_R	λ	f[a]	σ_R scale
Meta-X-Styrenes	-3.26	-1.11	0.34	0.12	σ_R^{BA}
Para-X-Styrenes	-2.80	-0.18	0.06	0.12	σ_R^-
Meta-X-β-Carbomethoxy-styrenes	-4.43	-0.94	0.09	0.12	σ_R^+
Meta-XCH_2-β-Carbomethoxy-styrenes	-1.93	-0.10	0.05	0.18	σ_R^-
Para-XCH_2-β-Carbomethoxy-styrenes	-1.79	0.03	-0.01	0.22	σ_R^-

[a] f = SD/RMS; f < 0.1 indicates a satisfactory correlation.

TABLE D-8

Comparison Between Experimental $^{13}C_{\alpha}$ SCS's and those Calculated Using the DSP Equation for Meta-X-Substituted-β-Carbomethoxystyrenes

Ring Substituent	SCS (C_{α}) Experimental	Calculated	Discrepancy
H	0.00	0.00	0.00
CH_3	0.23	0.41	+0.18
OCH_3	-0.01	-0.24	-0.23
OC_6H_5	-0.77	-0.16	+0.61
NMe_2	1.33	1.38	+0.05
F	-1.55	-1.68	-0.13
Cl	-1.86	-1.70	+0.16
Br	-1.86	-1.67	+0.19
I	-1.89	-1.49	+0.40
CF_3	-1.95	-2.07	-0.12
CN	-2.72	-2.60	+0.12
NO_2	-2.77	-3.02	-0.25

β-carbomethoxystyrenes gave an excellent linear correlation when plotted against each other (Figure 1(a)), the only serious discrepancy being for the $-CH_2CN$ substituent. When the same plot is drawn for the corresponding $^{13}C_\alpha$ data (Figure 2(a)) even the $-CH_2CN$ substituent is well behaved Examination of Figure 2(a) reveals that the only anomaly of any significance is for the $-CH_2OPh$ substituent and the SCS's for this substituent in other solvents (see Table D-5) suggest that it is in the para- value that the anomaly lies. In view of the low solubility of the phenoxy derivatives in ethanol, which necessitated working in extremely dilute solutions and consequently getting weak spectra, the most likely source of the discrepancy is experimental error.

The slope of the best line through the points in Figure 2(a) is close to unity. This is in contrast to the situation for the corresponding $^{13}C_\beta$ shifts (Figure 1(a)) where the chemical shifts were more sensitive to para- substituent effects than to substituent effects from the meta- position.

The $^{13}C_\alpha$ SCS's for the meta- and para- series of $X-CH_2-$ substituted β-carbomethoxystyrenes are shown plotted against Charton's σ_I values in Figures 2(b) and 2(c). These plots show a resemblance to those in Figure 1(b) and 1(c) for the corresponding data for the β-carbons. This similarity is confirmed by examining the graphs of the chemical shifts for the α-carbon against those for the β-carbon given in Figures 3(a) and 3(b). The substituents F, NMe_2, OMe, and OPh are all seen to deviate in Figures 2(b) and 2(c)

with approximately the same magnitude and in the same direction as they do in the C_β study. This is especially true in the meta series (see Figure 3(a)).

To summarize the above discussion concerning both the $^{13}C_\alpha$ and the $^{13}C_\beta$ measurements for the XCH_2- substituted β-carbomethoxystyrenes we can conclude the following:

(1) The total substituent effect of the XCH_2 group on the $^{13}C_\alpha$ and the $^{13}C_\beta$ shifts is similar in magnitude.

(2) The efficiency with which these substituent effects are transmitted to the α-carbon is almost independent of whether the side-chain is meta- or para- to the XCH_2 group. However this is not true for the transmission of these substituent effects to the β-carbon, suggesting the possibility that in the latter case resonance plays a more significant role.

(3) It is possible that substituent effects, other than those inductive or mesomeric in origin, influence both the $^{13}C_\beta$ and $^{13}C_\alpha$ SCS's in the same way. There may also be some of these "other substituent effects" which influence only the $^{13}C_\alpha$ SCS's.

1.3 ^{19}F NMR SUBSTITUENT CHEMICAL SHIFTS

Taft and co-workers[14] observed that the ^{19}F chemical shifts in meta- substituted fluorobenzenes appeared to be closely related to the inductive effect of substituents. This has since been criticized and it appears that resonance effects may not be entirely absent.[15] Taft also examined the effect of changing the solvent on these ^{19}F SCS's.

It was considered to be of interest for the purposes of this thesis to examine both the solvent effects and the substituent effects on ^{19}F SCS's of $\underline{XCH_2}$- substituted fluorobenzenes. The ^{19}F SCS's for both *meta*- and *para*- XCH_2- substituted fluorobenzenes were obtained from measurements made in five solvents, dimethylsulphoxide, acetone, deuterochloroform, carbon tetrachloride, and benzene. The data are reported in Table D-9.

It was not possible to record the ^{19}F SCS data in ethanol because many of the compounds were prone to rapid solvolosis in this solvent. Thus it is not possible to analyse this data in the same way as was done in 1.1 and 1.2 for the ^{13}C SCS data. However, it is possible to make the *meta*/*para* comparisons since any solvent can be used for this. The relevant data, recorded in acetone, are graphed in Figure 4(a). This correlation is poor by comparison with those obtained for the $^{13}C_\beta$ and $^{13}C_\alpha$ shifts (Figures 1(a) and 2(a) respectively) even though the data is much more accurate. This implies that the XCH_2 group is affecting the environment of the fluorine differently from the two positions. If these ^{19}F NMR data for the *meta*- and *para*- XCH_2- fluorobenzenes are compared with the corresponding $^{13}C_\beta$ data for the β-carbomethoxystyrenes (Figures 4(b) and 4(c)) then it seems that the ^{19}F SCS's for the *para*- series are being influenced by much the same properties as the *meta*- and *para*- series of $^{13}C_\beta$ SCS's but that some ^{19}F SCS's in the *meta*- XCH_2- substituted fluorobenzenes appear to be influenced by other factors. The

TABLE D-9

^{19}F NMR Substituent Chemical Shifts for

XCH_2- Substituted Fluorobenzenes

Ring Substituent	SCS (^{19}F) in Me_2SO	Me_2CO	$CHCl_3$	CCl_4	C_6H_6
3-CH_3	0.00	0.00	0.00	0.00	0.00
3-CH_3CH_2	0.24	0.20	0.24	0.28	0.26
3-CH_3OCH_2	0.68	0.65	1.02	0.76	0.78
3-$C_6H_5OCH_2$	0.98	1.02	1.48	1.37	1.20
3-$(CH_3)_2NCH_2$	0.39	0.30	0.85	0.34	0.33
3-FCH_2	1.29	1.18	1.62	1.56	1.30
3-$ClCH_2$	1.22	1.30	1.79	1.65	1.40
3-$BrCH_2$	1.22	1.30	1.86	1.73	1.49
3-ICH_2	1.18	1.33	1.89	1.77	1.47
3-$NCCH_2$	1.59	1.76	2.68	2.52	1.98
3-O_2NCH_2	1.33	1.58	2.78	2.68	2.08
4-CH_3	0.00	0.00	0.00	0.00	0.00
4-CH_3CH_2	0.44	0.33	0.37	0.43	0.37
4-CH_3OCH_2	3.17	3.11	3.74	3.05	3.11
4-$C_6H_5OCH_2$	3.86	3.76	4.31	3.86	3.83
4-$(CH_3)_2NCH_2$	2.42	2.54	3.09	2.29	2.49
4-FCH_2	5.35	5.32	5.80	5.24	5.17
4-$ClCH_2$	4.86	4.98	5.36	4.97	4.80
4-$BrCH_2$	5.10	5.13	5.69	5.31	5.09
4-ICH_2	4.41	4.70	5.22	4.86	4.67
4-$NCCH_2$	3.51	3.72	4.76	4.35	3.87
4-O_2NCH_2	6.49	6.76	8.14	7.63	7.04

TABLE D-10

^{19}F Substituent Chemical Shifts[14] for Meta-X-Substituted Fluorobenzenes

Ring Substituent	SCS (^{19}F) in MeOH	Me_2SO	Me_2CO	CCl_4	C_6H_6
H	0.00	0.00	0.00	0.00	0.00
CH_3	-1.15	-1.05	-1.13	-1.18	-1.15
OCH_3	1.38	1.30	1.28	1.05	1.18
OC_6H_5	2.05	2.10	2.13	1.95	2.20
F	3.38	3.13	3.20	3.03	3.08
Cl	2.38[a]		2.34[a]		
Br	2.63	2.63	2.65	2.30	2.60
I	2.66[a]		2.62[a]		
CF_3	2.50	2.33	2.38	2.13	2.28
CN	3.10	2.58	2.80	2.75	2.75
NO_2	3.60	3.15	3.40	3.45	3.25

[a] - This data is from the work of Hirst, J., and Una, S.J., J. Chem. Soc., (B), 1969, p.646.

The para- data correlate well with the exception of that for the $-CH_2CN$ substituent. Recall however, that the $^{13}C_\beta$ shift for this substituent in the para- position appeared upfield of its expected position. This anomaly is even more pronounced in the ^{19}F SCS's of the para- XCH_2- fluorobenzenes. Notice also that again the shift for the meta- CH_2F substituent relative to those for $-CH_2Cl$, $-CH_2Br$ and $-CH_2I$ is different to that expected on the basis of the normally accepted inductive order for the halogens.

If the data for the XCH_2- substituted fluorobenzenes are compared with Tafts ^{19}F data[14] for the meta-X-fluorobenzenes (relevant data from Taft's study are contained in Table D-10) then correlations are poor. Figures 5(a) and 5(b) show graphs of the ^{19}F SCS values and it can be seen that the observed deviations are clearly too large to be attributable to experimental error. Figure 5(c) shows that, on the other hand, Taft's data recorded in methanol do not correlate all that well with Carton's σ_I values either.

A major difference between the meta- X ^{19}F data and the $-CH_2X$ data is that in the former the fluoro substituent has a SCS which is much more in accordance with its predicted electronic effect. That is, that the "other substituent effect", noted for the CH_2X data, does not appear to be operating in the meta-X-fluorobenzenes. However, in the meta-X-fluorobenzenes the methyl substituent shows as a serious anomaly and the quantitative position of the fluoro substituent relative to the cyano and nitro is not what is normally expected either.

To summarize the entire discussion thus far: For none of the series investigated can it be stated unequivocally that the substituent chemical shifts observed are influenced solely by the inductive effect of the substituents. In some cases the observed discrepancies appear to be due to resonance (for example, in the $^{13}C_{\alpha}$ data for the X-substituted styrenes and β-carbomethoxystyrenes) while in other cases the unexpected shifts appear to be substituent specific (for example $-CH_2F$ and $-CH_2CN$). However, it can be said that in each series the inductive effect of the substituent is the dominating influence on the substituent chemical shift. On the basis of this last conclusion the next section will examine the influence of solvent on these SCS's in an attempt to establish the effect of solvent on σ_I

2. SOLVENT EFFECTS

In the series discussed so far there are a number of factors that can influence substituent chemical shifts. These can be separated into substituent effects, transmission effects and solvent effects. It is convenient for our purposes in this discussion to further subdivide substituent effects into three types.

(i) Those which arise as a result of a conjugate interaction between the substituent and the atom whose resonance is being measured; their magnitudes can be discussed in terms of σ_R values for the substituent.

(ii) Those that affect the chemical shift by a purely electrostatic effect; their magnitudes are reflected as σ_I values for the substituents.

(iii) Other substituent effects whose origin cannot be assigned with certainty.

Transmission effects represent the efficiency with which substituent effects are relayed from the substituent to the atom whose resonance frequency is being measured. To maintain our analogy with the Hammett equation their magnitudes will be expressed in terms of ρ values.

The solvent medium is capable of influencing both substitutent effects and transmission effects. Thus a substituent chemical shift arises from a combination of a substituent effect, a transmission effect, and a solvent effect on each of these. The first problem in interpreting the effect of solvent on SCS is in apportioning

the observed effect into changes in the substituent effect and changes in the transmission efficiency. Even if this barrier can be crossed, we then meet another. How can we apportion the solvent dependence of substituent effects into the individual dependences of σ_I (our major interest), σ_R, and other substituent effects? It is fairly clear that in the latter case we should concentrate on systems for which substituent effects, other than inductive effects, are as small as possible, since this means any solvent dependence they have on SCS will be small. It should also be apparent from the first part of the discussion that our success in this regard has not been all we would have wished. In these circumstances the best approach is to examine all the available data and to try and establish areas where the results agree fairly well with one another.

Series available in which the bulk of the evidence suggests that the observed substituent effect of X is dominated by its inductive effect for most X are:

(i) meta-X-substituted β-carbomethoxystyrenes (both $^{13}C_\alpha$ and $^{13}C_\beta$).

(ii) meta- and para- XCH_2-substituted β-carbomethoxystyrenes (both $^{13}C_\alpha$ and $^{13}C_\beta$).

(iii) meta- and para- XCH_2-substituted fluorobenzenes (^{19}F).

In addition it is possible to make use of the measurements of Taft and co-workers[14] on

(iv) meta-X-substituted fluorobenzenes (^{19}F).

Of these the resonance effect of X definitely makes a contribution to the SCS in (i) and probably (iv), and

other unknown substituent effects appear to play significant roles in all but the $^{13}C_{\beta}$ data in (i).

The first problem that needs to be tackled however is that of resolving solvent effects into transmission effects and substituent effects. This problem was discussed by Happer in his study[21] of the solvent dependence of SCS for $^{13}C_{\beta}$ of the styrenes. He observed that for the three meta-halogeno substituents F, Cl and Br, that SCS's were about 20% greater in 75% ethanol, ethanol, Me_2SO, and acetone than they were in $CDCl_3$, CCl_4 and benzene. He tentatively ascribed this to a solvent effect on σ_I rather than on ρ, but the supporting evidence was weak. If this were indeed true then similar behaviour should be noted for all of series (i) - (iv) since in all of these the inductive effect is the major component of the substituent effect. A survey of Tables D-1 to D-6, D-9 and D10 shows that this is not true, and that of those listed, it is only the SCS data for C_{β} of meta-X-substituted styrenes and β-carbomethosystyrenes that show this form of solvent dependence. In the others the solvent dependence of SCS for the halogeno substituents is in general, relatively slight and, where it is found, random. For this reason, in the following discussion it has been assumed that the substituents H, Me, F, Cl and Br show negligible solvent dependence of σ_I. This simplifies the discussion considerably since the solvent dependence of transmission effects can now be defined and that of substituents considered in terms of variations from their value pertaining to ethanol.

In the discussion that follows the approach has been to first consider the effect of solvent on the $^{13}C_{\alpha}$ and $^{13}C_{\beta}$ SCS's of the XCH_2-substituted β-carbomethoxystyrenes, since these are the only series in which the resonance effect of X is likely to make no contribution and for which we have data in all solvents. This is followed by a discussion of the ^{19}F data, including that of Taft. This is kept separate because ethanol data could not be used as a basis of comparison, and in the case of the meta-X-substituted fluorobenzenes contributions from sources other than inductive effects could have been present.

Lastly we look at the two cases where other effects are known to make significant contributions - the $^{13}C_{\alpha}$ and $^{13}C_{\beta}$ chemical shifts of the β-carbomethoxystyrenes.

Finally the whole is gathered together and an attempt is made to come up with sets of σ_I and σ^{meta} values that can be used for the various solvents studied.

2.1 SOLVENT-SCS CORRELATIONS IN THE XCH_2-SUBSTITUTED β-CARBOMETHOXYSTYRENES

Note.

It should be pointed out that in these series measurement errors are quite large relative to the magnitudes of the inductive effects. Variations of ±0.05 ppm may be considered normal and these correspond to changes in σ_I of 0.02 - 0.03 units.

2.1.1 Dimethylsulphoxide.

The data for the $^{13}C_{\alpha}$ and $^{13}C_{\beta}$ of the meta- and para-XCH_2- substituted β-carbomethoxystyrenes in dimethylsulphoxide graphed against the same data in ethanol are shown in Figures 6(a) - 6(d). The results for the four series are not in total agreement. The position of the line can be drawn with more confidence in the C_{β} cases since there is less scatter and it should be remembered that the origin of the shifts is better understood for these also.

Both sets of $^{13}C_{\beta}$ data suggest lower values of σ_I for the -CN and $-NO_2$ substituents apply in dimethylsulphoxide than in ethanol. The $^{13}C_{\alpha}$ data support a lower value for cyano- but not for nitro-.

For the methoxy-, phenoxy- and dimethylamino-substituents there is some scatter but it appears that the σ_I value for the $-NMe_2$ group at least, should be lower in dimethylsulphoxide than in ethanol. The discrepancy for the -OPh substituent in the para- XCH_2- $^{13}C_{\alpha}$ graph is probably due to an error in the ethanol value (methyl para-phenoxymethyl cinnamate had very limited solubility in ethanol) as a similar discrepancy is observed for this substituent for all of the other solvents as well. The four plots agree with a slightly smaller value of σ_I for the -OMe group in dimethylsulphoxide than in ethanol but the difference is almost insignificant.

The iodo-substituent appears to follow the other halogeno substituents and shows no solvent dependence here.

2.1.2 Acetone.

Acetone, like dimethylsulphoxide, may be considered a dipolar aprotic solvent, although less dipolar than the former. It might, therefore, be expected to show a similar but weaker solvent effect. Graphs of the acetone data against that for ethanol are given in Figures 7(a) - 7(d).

The predicted similarity of behaviour between acetone and dimetylsulphoxide is basically supported. The behaviour of the cyano-, nitro- and dimethylamino- groups is very similar in both solvents but the iodo- substituent however, appears to be behaving as a slightly stronger inductive electron withdrawer in acetone than in either ethanol or dimethylsulphoxide. The methoxy- and phenoxy- substituents exhibit much the same behaviour in acetone as they showed in dimethylsulphoxide.

2.1.3 Deuterochloroform.

Deuterochloroform is a very different solvent in character from either dimethylsulphoxide or acetone. It is relatively non-polar and much more weakly hydrogen bonding than either water or ethanol. Graphs of the $CDCl_3$ data against that for ethanol are given in Figures 8(a) - 8(d).

In contrast to the situation for acetone and dimethylsulphoxide all four plots seem to be in reasonable agreement with each other. For deuterochloroform the values of σ_I for the cyano- and nitro- substituents appear to be significantly larger than in ethanol. The dimethylamino group appears to have a σ_I value as much as 0.1 σ_I units

lower than in ethanol. Any other deviations observed cannot be distinguished from measurement errors.

2.1.4 Carbon Tetrachloride.

Carbon tetrachloride is the least polar of the solvents used in this study but we would not expect solvent effects to differ much in this solvent from those observed for $CDCl_3$. The graphs against ethanol are given in Figures 9(a) - 9(d).

Figures 9(a) - 9(d) bear a fair resemblance to the deuterochloroform ones especially in so far as the cyano- and nitro- groups are concerned. For these substituents we find that their σ_I values in CCl_4 should be about 0.03 σ_I units higher than in ethanol. For the dimethylamino- group the deviation is very large suggesting that this substituent should have a σ_I value which is about 0.15 units lower than it has in ethanol. This change is 50% greater than that found in deuterochloroform which implies that some interaction between the $-NMe_2$ group and the solvent exists for both $CDCl_3$ and ethanol. The direction of the change is consistent with an increase in σ_I due to hydrogen bonding to the amine nitrogen which would result in an increase in the effective positive charge on the nitrogen and the resultant increase in σ_I with increasing hydrogen bonding ability of the solvent.

The methoxy- group shows an effect similar in direction to the dimethylamino group in this solvent. The magnitude of the deviation corresponds to a decrease in σ_I in carbon tetrachloride of 0.05 - 0.1 units from that

in ethanol. Changes approaching this magnitude were not observed for the methoxy substituent in either acetone or dimethylsulphoxide. These solvents, like carbon tetrachloride, would not be expected to interact significantly with a methoxy substituent. By way of contrast, the phenoxy substituent shows a similar substituent chemical shift in carbon tetrachloride and ethanol.

2.1.5 Benzene.

Benzene is a non-polar solvent with no permanent dipole moment, but unlike carbon tetrachloride it has a polarizable π system that could affect interactions with dipolar molecules. In practice we find its effect on chemical shifts significantly different from that of carbon tetrachloride. The graphs of the benzene data against the ethanol data are given in Figures 10(a) - 10(d).

It can be seen in Figures 10(a) - 10(d) that the benzene data correlates particularly well with the ethanol data. This is most noticeable for the $^{13}C_{\beta}$ SCS's. The only obvious deviation is that once again the dimethylamino substituent appears to have a σ_I value around 0.1 (for the $^{13}C_{\beta}$ data) to 0.15 (for the $^{13}C_{\alpha}$ data) lower than that for ethanol. This would again be consistent with increased hydrogen bonding in the ethanol solvent. Notice also that the $^{13}C_{\alpha}$ data suggest that σ_I for the substituents cyano- and nitro- should be very slightly larger in benzene than in ethanol although this is not found for the C_{β} graphs.

2.1.6 Summary of Solvent Effects on σ_I Based on the XCH_2-substituted β-Carbomethoxystyrenes.

H,Me,F,Cl,Br : The use as a standard seems justified in that variations are small enough to be due to experimental error.

I- : Shows very little solvent dependence.

-OMe,-OPh : Any consistent solvent dependence cannot be easily distinguished from measurement errors.

$-NMe_2$: In all cases values for σ_I lower than that for ethanol were indicated. For acetone and dimethysulphoxide the difference was small (about 0.03 σ_I units) but for the non-polar solvents changes of -0.1 ($CDCl_3$ and C_6H_6) or even -0.15 (CCl_4) σ_I units are indicated. The SCS's for this substituent in ethanol are very high (see Tables D-2 and D-5) suggesting an apparent σ_I value of about 0.27 which can be compared with Charton's figure of 0.17. The apparent σ_I values for the NMe_2 group are therefore also high in dimethylsulphoxide and acetone.

$-CN,-NO_2$: These polar substituents exhibited consistent solvent effects. The dipolar aprotic solvents (acetone and dimethylsulphoxide) caused an apparent reduction in σ_I of about 0.05 units relative to ethanol while the non-polar solvents deuterochloroform and carbon tetrachloride, caused an apparent increase in σ_I of about 0.03 units. The figure for benzene was about the same as for ethanol.

2.2 SOLVENT-SCS CORRELATIONS IN THE FLUOROBENZENES

The conclusions, based on ^{13}C NMR chemical shifts of both the α- and β- carbons in meta- and para- XCH_2- substituted β-carbomethoxystyrenes, can be tested by comparison with data for other NMR substituent chemical shifts.

2.2.1 ^{19}F NMR Shifts of XCH_2 Substituted Fluorobenzenes

Since ^{19}F SCS data were not available in ethanol it was not possible to carry out the same treatment as was applied to the ^{13}C data. However, it transpired from the latter data that the two solvents benzene and ethanol behave very similarly toward the substituents involved in this study for all but the dimethylamino substituent. Thus if the rest of the XCH_2- ^{19}F data are compared to that in benzene conclusions similar to those arrived at in the ^{13}C NMR should result. Graphs of this data for dimethylsulphoxide, acetone, chloroform and carbon tetrachloride are shown for both the meta- series (Figures 11(a) - 11(d)) and the para- series (Figures 12(a) - 12(d)). Since the ^{19}F shifts can be measured with greater accuracy and the range of the SCS's is greater, the experimental uncertainties are much less than for the ^{13}C SCS's for the methyl cinnamates. An examination of the figures 11 and 12 reveals, however, that in the ^{19}F study we appear to have failed to eliminate the unknown "other substituent effects". For example, in both the meta- and para- series the methyl substituent appears to be behaving as a slight electron withdrawer and in the meta- series in the solvents dimethylsulphoxide

and acetone, the nitro- substituent seems to have lost some of its power as an inductive electron withdrawer. It, therefore, seems that changes in solvent are affecting these "other substituent effects".

All in all, however, these results do provide support for the ^{13}C NMR investigation. They show also that the unknown factors that influenced the $-CH_2F$ and $-CH_2CN$ ^{13}C NMR substituent chemical shifts are also influencing the ^{19}F shifts. For the latter shifts, the unknown substituent effect is even more evident although not obviously affected by solvent. The greater accuracy of the ^{19}F data permits a closer study of the solvent dependence of the dimethylamino, methoxy- and phenoxy SCS's. However, there are conflicts between the meta- and para- data and changes are neither great nor readily predictable.

2.2.2 ^{19}F NMR Shifts of Meta-X-Substituted Fluorobenzenes.

It is clearly of interest to compare conclusions on the solvent dependence of σ_I based on Taft's ^{19}F data[14] for the meta-X-flurorbenzenes with conclusions based on the ^{19}F and ^{13}C NMR data presented here. Unfortunately, Taft's study did not include some of the substituents included in our study and neither did they investigate the solvent ethanol. They did, however, obtain values for the shifts in methanol so this solvent will be used as a basis for comparison where ethanol was used in the above discussion. The reliability of his SCS data was estimated by Taft to be ±0.08 ppm which is of substantially lower reliability

than that of the $-CH_2X$ ^{19}F data.

Graphs of the SCS's of the meta-X-fluorobenzenes in dimethylsulphoxide, acetone, carbon tetrachloride and benzene against the same shifts in methanol are shown in Figures 13(a) - 13(d). The best lines are drawn through the points corresponding to the substituents H, CF_3, Br and F. The methyl substituent is not used as a solvent independent standard because the SCS's for this substituent are so anomalous as not to warrant inclusion (they would be well off the graphs to the left). The data for the $-CF_3$ substituent has been included in our solvent independent basis set since only two of the four halogens were covered by Taft. In Happer's investigation of the solvent dependences of $^{13}C_\beta$ SCS's in styrenes,[21] the trifluoromethyl substituent showed a similar solvent dependence to the halogens.

Consideration of the graphs in Figure 13 confirms, to some extent, the conclusions previously drawn. In dimethylsulphoxide the cyano- and nitro- substituents are less electron withdrawing than in methanol. In acetone this is true for the cyano- substituent although the difference is small enough for the observed discrepancy to be accounted for by experimental error. In carbon tetrachloride the nitro- substituent seems to be more electron withdrawing than in methanol as was observed for the other systems. However, the cyano- substituent shows no deviation in this solvent. Finally, as was observed before in benzene, both the nitro- and cyano-

substituents behave the same as in the alcoholic solvent.

In Taft's data, the methoxy group is seen to require a lower σ_I value in other solvents relative to methanol while the phenoxy group consistently requires a higher σ_I. These observations are difficult to rationalize. Although no data is given for particular solvents, the dimethylamino substituent has a much lower apparent σ_I value in non-polar solvents relative to methanol, just as was observed for data presented earlier in this thesis.

2.3 SOLVENT-SCS CORRELATIONS IN THE META-X-SUBSTITUTED β-CARBOMETHOXYSTYRENES

2.3.1 Substituent Chemical Shifts of the β-Carbon.

As discussed in section 2.1 the $^{13}C_\beta$ SCS's for the meta-X-substituted styrenes and β-Carbomethoxystyrenes, where X is H-, Me-, F-, Cl- and Br-, should be free from both solvent effects and unknown substituent effects. The rest of the substituents in this study do not appear to exert unknown substituent effects in these series but some do show solvent dependences. Unfortunately these solvent effects will be a combination of the solvent effects of σ_R^{meta} and of σ_I. The data for the meta-X-substituted β-carbomethoxystyrenes has here been treated in the same manner as the previous data and the graphs for the shifts in dimethylsulphoxide, acetone, deutero-chloroform, carbon tetrachloride and benzene against those in ethanol are given in Figures 14(a) - 14(e)). It may be recalled that these shifts correlate with excellent

precision with the corresponding styrene shifts so that a separate analysis for the styrene data would be superfluous.

If it is assumed that σ_R^{meta} is approximately independent of solvent then examination of Figures 14(a) - 14(e) leads to the same conclusions as those drawn from the data for other series. The shifts in dimethylsulphoxide and acetone for the cyano- and nitro- substituents lead to predicted σ_I values that are lower than those in ethanol by about 0.06 σ_I units. In deuterochloroform and carbon tetrachloride the indicated σ_I values for these substituents are higher by about 0.04 units, and in benzene they are about the same as in ethanol.

Since these meta-X-substituent chemical shifts show solvent dependences much the same as those observed for the XCH_2- SCS and other NMR data dominated by inductive effects, the assumption that σ_R^{meta} is roughly independent of solvent seems to have been justified. The validity of this assumption is discussed later (section 2.5).

2.3.2 Substituent Chemical Shifts of the α-Carbon

It would not be surprising if the effect of solvent on σ_I was obscured in this series since, although the $^{13}C_\alpha$ shifts are dominated by inductive substituent effects, other unknown substituent effects are also present and the part played by resonance is unclear. The appropriate graphs for this series are given in Figures 15(a) - 15(e).

The correlations are good for all substituents indicating a relatively small effect of solvent on these shifts. The substituents cyano- and nitro- still show small solvent effects in the same direction as in all the other series although the magnitude of these effects is much smaller than usual in dimethylsulphoxide and acetone. In addition the substituent effect of these substituents is slightly different in benzene from that in ethanol. This is contrary to what we have come to expect from all the other series and is thus unlikely to be due to solvent effects on σ_I.

Again no consistent solvent effect on the methoxy- and phenoxy- substituents is observed. The dimethylamino group has SCS values which are more positive in the less hydrogen bonding solvents dimethylsulphoxide, acetone, carbon tetrachloride and benzene. This is consistent with the earlier interpretation of the effect of solvent on this substituent when it is remembered that $^{13}C_\alpha$ SCS's exhibit reversed substituent effects. The solvent deuterochloroform appears as an unexplained anomaly with the $-NMe_2$ group in this series since a σ_I value greater than in ethanol is indicated.

2.4 THE EFFECT OF SOLVENT ON THE SENSITIVITY OF NMR SCS'S TO CHANGES IN SUBSTITUENT EFFECTS

In investigating the solvent dependence of σ_I the assumption was made that the σ_I values for the substituents H-, Me-, F-, Cl- and Br- were in fact independent of solvent.

Although this has not been proved, and indeed would be extremely difficult to prove, none of the data available gives any reason to suspect that this assumption is wrong. The procedure in the preceding investigation was to plot SCS data obtained in other solvents against that obtained in ethanol, drawing the best line through the basis set of shifts assumed to be solvent independent. The slope of all these plots is then a measure of the effect of solvent on the sensitivity of the shifts to changes in substituent relative to ethanol. These solvent induced changes in slope (ρ) are summarized in Table D-11.

It can be seen that the data in Table D-11 show no overall patterns. If σ_I values for the basis set of substituents were markedly influenced by any one solvent then this would be reflected in Table D-11 by ρ values consistently different from unity for this one solvent. This is clearly not the case.

2.5 THE SOLVENT DEPENDENCE OF σ^m and σ_I.

Our survey of the solvent dependence of SCS for the various series showed that while all series had their defects, at least for some substituents certain consistencies in behaviour did arise. On the basis of our assumption that σ_I for H, Me, F, Cl and Br was solvent independent there was substantial agreement between series as to the solvent dependence of σ_I for the -CN and $-NO_2$ groups. The results indicated that these were about the same in benzene as in ethanol but higher in CCl_4 and $CDCl_3$ and lower in Me_2SO and

TABLE D-11

The Effect of the Solvent on Sensitivity to Substituent Effects.

Series	ρ solvent / ρ_{EtOH} for EtOH	Me_2SO	Me_2CO	$CDCl_3$ (or $CHCl_3$)	CCl_4	C_6H_6
m-$XCH_2(C_\beta)$	1.00	0.9	1.0	1.1	1.05	0.85
p-$XCH_2(C_\beta)$	1.00	1.0	1.05	1.01	1.0	0.90
n-$XCH_2(C_\alpha)$	1.00	0.9	0.95	1.15	1.1	1.15
p-$XCH_2(C_\alpha)$	1.00	0.8	0.9	1.05	0.9	1.0
m-$XCH_2(^{19}F)$ [a]		0.8	0.9	1.25	1.2	1.00
p-$XCH_2(^{19}F)$ [a]		1.00	1.0	1.1	1.05	1.00
m-$X(^{19}F)$ [b]		0.9	0.95		0.9	0.9
m-$X(C_\beta)$	1.00	0.98	1.00	0.86	0.86	0.70
m-$X(C_\alpha)$	1.00	0.90	0.93	0.93	0.92	1.00

[a] - relative to benzene = 1.00

[b] - relative to methanol = 1.00

Me_2CO. Such conclusions have important implications if we examine more closely the possible solvent dependence of σ_R^{meta}, which in section 2.3.1 was suggested to be at least approximately solvent independent. If Happer's data for styrenes are considered in the light of the assumption that σ^{meta} for H, Me, F, Cl and Br is solvent independent, then it is found that σ_R^{para} for these varies with solvent. The differences between their values in ethanol, dimethyl sulphoxide and acetone on the one hand and deuterochloroform, carbon tetrachloride and benzene on the other are quite significant. If we assume $\rho^{meta} = \rho^{para}$ then the solvent dependence of $(\sigma_R^{para} - \sigma_R^{meta})$ can be examined in isolation. Not let us relax our assumption regarding the solvent dependence of σ_R^{meta} and replace it by one that says merely that the ratio $\sigma_R^{meta}/(\sigma_R^{para} - \sigma_R^{meta})$ H, Me, F, Cl and Br is solvent independent (i.e., solvent effects on σ_R^{meta} and σ_R^{para} are proportionally equivalent). This is probably as good an estimate as we can make in the circumstances. The values of these ratios for these substituents can be obtained from the ethanol data, using Charton's[47] σ_I and σ^{meta} values. It now becomes possible to derive improved values for σ^{meta} for use in solvents other than ethanol. These can in turn be used to calculate improved ρ values and new values for $(\sigma_R^{para} - \sigma_R^{meta})$. This process can be repeated until σ^{meta} and hence ρ no longer changes. These final set of ρ values can then be used to calculate σ^{meta} and σ^{para} for all substituents. Lastly, by using the same

assumption as before as to the solvent independence of $\sigma_R^{meta}/(\sigma_R^{para} - \sigma_R^{meta})$ we can calculate σ_I values for the other substituents (OMe, CF_3, CN, NO_2) in the various solvents. The result of such a series of calculations are given in Table D-12. Values in parentheses are ones based on the assumption that σ_R^{meta} is solvent independent.

It may be noted that the greatest differences are found in the lower right part of the Table. The values in parentheses reflect to a very much greater degree than the others, the sorts of trends observed in the other series. Of the two, they alone are consistent with the observation that σ_I for the -CN and $-NO_2$ groups is higher in $CDCl_3$ and CCl_4 than in ethanol, and about the same in benzene. This must be considered as extremely strong evidence for the insignificant solvent dependence of σ_R^{meta} over the range of solvents studied.

Such an observation is extremely valuable in that it allows us to use these $^{13}C_\beta$ data alone to ascertain the solvent dependence of σ^{meta} and σ_I. These, of course, have the advantage of constituting a series where substituent effects, other than inductive and resonance ones, appear negligible.

This method can be improved further by incorporating other available $^{13}C_\beta$ data for similarly substituted styrenes bearing other β- substituents, since this tends to minimize random errors. The series used are summarized in Table D-13. Most of the data is for the

TABLE D-12

Calculated[a] σ_I values based on C_β data for Styrenes in solvent

Substituent	75% EtOH	EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
OMe	0.27 (0.27)	0.23 (0.23)	0.25 (0.24)	0.23 (0.23)	0.26 (0.25)	0.23 (0.24)	0.26 (0.25)
CF_3	0.43 (0.43)	0.44 (0.43)	0.41 (0.41)	0.41 (0.40)	0.40 (0.43)	0.44 (0.46)	0.41 (0.43)
CN	0.62 (0.62)	0.62 (0.61)	0.53 (0.54)	0.54 (0.54)	0.61 (0.65)	0.64 (0.67)	0.54 (0.57)
NO_2	0.67 (0.67)	0.67 (0.66)	0.59 (0.61)	0.63 (0.62)	0.69 (0.74)	0.69 (0.72)	0.61 (0.65)

[a] Values in parenthesis are based on the assumption that σ_R^{meta} is solvent independent while the others assume slight solvent dependences are possible for this substituent constant.

TABLE D-13

Series Used to Determine σ^{meta} Constants

β Substituent	Solvents	Reference
-Ac	$CDCl_3$	This work
Br (cis- & trans-)	$CDCl_3$	This work
2-C_5H_4N, 4-C_5H_4N	$CDCl_3$	84
2-C_5H_4NMeI, 4-C_5H_4NMeI	Me_2SO	84
CN (cis- & trans-)	$CDCl_3$	This work
CN/CN	Me_2SO	23
COO^-	H_2O	23
CO_2H	Me_2SO	23
CO_2Me	EtOH,Me_2So,Me_2CO,$CDCl_3$,CCl_4,C_6H_6	This work
H	75% EtOH,EtOH,Me_2So,Me_2CO,$CdCl_3$,CCl_4,C_6H_6	21
$MeSO_2$	$CDCl_3$	This work
$MeSO_2/CO_2Et$	$CDCl_3$	This work

deuterochloroform but there is a certain amount for dimethylsulphoxide as well. All of the data from these series can be combined to give the best set of σ^{meta} values for the basis set of substituents.

The basis set of σ values chosen as standards are:

Substituent	H	Me	F	Cl	Br
σ^{meta}	0.00	-0.06	0.34	0.37	0.39

The finally derived σ^{meta} values listed in Table D-14 are based on ρ values determined from the $^{13}C_{\beta}$ shifts of the series in Table D-13 and the solvent independent σ^{meta} values for the basis set of substituents. Differences of 0.01 σ units normally correspond to about 0.04 ppm variations in chemical shift and so are not significant.

σ_I values can be calculated from the σ^{meta} values of Table D-14 simply by subtracting σ_R^{meta} which has been assumed to be solvent independent. The calculated σ_I values are given in Table D-15. (The σ_R^{meta} values used were obtained from Charton's[47] σ_I and σ^{meta} data).

The σ^{meta} and σ_I values listed in Tables D-14 and D-15 are used in the next section of this discussion to investigate the effect on σ_R^{para} of changing the β-substituent in β- substituted styrenes.

TABLE D-14

σ^{meta} Constants in Various Solvents

Substituent	H_2O[a]	EtOH[b]	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
3-CH_3	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06
3-OCH_3	0.11	0.04	0.07	0.05	0.07	0.04	0.06
3-F	0.34	0.35	0.35	0.35	0.35	0.34	0.36
3-Cl	0.37	0.37	0.38	0.38	0.37	0.37	0.38
3-Br	0.39	0.38	0.38	0.38	0.38	0.38	0.37
3-CF_3	0.46	0.50	0.49	0.49	0.50	0.51	0.49
3-CN	0.61	0.64	0.58	0.57	0.69	0.68	0.61
3-NO_2	0.74	0.74	0.67	0.68	0.79	0.77	0.72
3-NMe_2	-0.16	-0.19	-0.16	-0.18	-0.15	-0.18	0.16
3-OPh	0.23	0.19	0.20	0.21	0.24	0.24	0.22
3-I	0.35	0.33	0.31	0.32	0.32	0.34	0.33

a These are the values listed by Charton.[47]

b σ^{meta} values for 75% EtOH/H_2O were identical to those for EtOH except for the meta = OCH_3 substituent for which a higher value of + 0.08 was needed.

c The σ^{meta} values for these substituents in solvents other than water being based on only one system (C_β for the meta-X-β-carbomethoxystyrenes) are less reliable than the others.

TABLE D-15

Calculated σ_I Constants in Various Solvents

Substituent	H_2O[a]	EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
CH_3	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01
OCH_3	0.30	0.23	0.26	0.24	0.26	0.23	0.25
F	0.54	0.55	0.55	0.55	0.55	0.54	0.56
Cl	0.47	0.47	0.48	0.48	0.47	0.47	0.48
Br	0.47	0.47	0.46	0.46	0.46	0.46	0.45
CF_3	0.40	0.44	0.43	0.43	0.44	0.45	0.43
CN	0.57	0.60	0.54	0.53	0.65	0.64	0.57
NO_2	0.67	0.67	0.60	0.61	0.72	0.70	0.65
NMe_2[b]	0.17	0.14	0.17	0.15	0.18	0.15	0.17
OPh[b]	0.40	0.34	0.35	0.36	0.39	0.39	0.37
I[b]	0.40	0.38	0.36	0.37	0.37	0.39	0.38

[a] These values were listed by Charton.[47]

[b] The σ_I values for these substituents in solvents other than water being based on only one system (C_β for the meta-X-β-carbomethoxystyrenes are less reliable than the others.

3. β-SUBSTITUENT EFFECTS

The introduction of a constant β-substituent or substituents into a series of meta- and para- substituted styrenes significantly affects both the $^{13}C_{\alpha}$ and $^{13}C_{\beta}$ NMR substituent chemical shifts. The β- substituent can have an effect on both the sensitivity of these SCS's to changes in the ring substituent and the magnitude of the resonance interaction between para- substituents and the side-chain. The change in β- substituent does not, however, affect the degree of resonance interaction between a meta- substituent and the side-chain. In addition, if the β- substituent is cis- to the aromatic ring rather than trans-, then both σ_R^{para} and ρ may change, possibly as a result of the changes in the ability of the ring and side-chain to attain coplanarity.

In order to examine these effects, meta- and para- substituted series of styrenes with eight different β- substituents were prepared and their ^{13}C NMR spectra obtained in deuterochloroform. These data were supplemented by similar data on eight further series of β- substituted styrenes either previously reported in the literature or available in the department.

The meta- substituents used to define ρ in the $^{13}C_{\beta}$ study were Me, OMe, F, Cl, Br, CF_3, CN and NO_2. In so far as the para- substituents were concerned, the preferred set were NMe_2, OMe, Me, F, Cl, Br, CN, and NO_2 but it was not always possible to prepare the full set. Emphasis was

placed on +R substituents because (a) the derivatives bearing these substituents were very much easier to prepare and (b) most of the β-substituents used were -R ones (they also were by far the easiest made), and situations where substituents and side-chains were capable of resonance interaction with each other were considered of greatest interest. In the case of series obtained from other sources the choice of substituents was beyond our control, as were the conditions of the measurements (many were made in much more concentrated solutions than we would wish). Only data measured in $CDCl_3$ solvent were considered, since this prevented trends being possibly obscured by solvent effects.

3.1 THE EFFECT OF THE β-SUBSTITUENT ON σ_R^{para} for +R RING SUBSTITUENTS

The $^{13}C_\beta$ NMR SCS's for the meta- substituents of each series were correlated with the σ^{meta} values of Table D-14. The ρ values obtained were used to calculate σ^{para} values, ρ_{meta} being assumed to be equal to ρ_{para}; σ_R^{para} for each of the substituents was then calculated simply by subtracting the appropriate σ_I values in Table D-15. The σ_R^{para} values calculated from experimental data obtained in this study are summarised in Table D-16; σ_R^{para} values calculated from literature SCS data are given in Table D-17.

The first observation we can make is that it is possible to rank the β- substituents in order of their ability to increase $|\sigma_R|$ of the para +R substituents.

TABLE D-16

Variation of σ_R^{para} and ρ_{meta} with β-Substituent in $CDCl_3$ (Current investigation)

	σ_R^{para} for β-Substituent [a]							
Ring Substituent	Br	Br(Cis)	CO_2Me	$MeSO_2$	CN	CN(cis)	Ac	$MeSO_2/CO_2E+$
4-NMe_2	-1.25	-	-1.59	-1.74[b]	-1.69	-1.70	-1.91	-2.18
4-OMe	-0.80	-0.75	-0.89	-0.92	-0.91	-0.92	-1.04	-1.06
4-Me	-0.23	-0.19	-0.26	-0.27	-0.27	-0.26	-0.32	-0.32
4-F	-0.63	-0.57	-0.60	-0.59	-0.59	-0.61	-0.66	-0.61
4-Cl	-0.32	-0.27	-0.32	-0.33	-0.32	-0.33	-0.35	-0.34
4-Br	-0.28	-0.23	-0.30	-0.31	-0.29	-0.29	-0.33	-0.34
4-CN	0.30	0.20	0.28	0.22[b]	-	-	-	-
4-NO_2	0.41	0.28	0.45	0.22[b]	0.29	0.25	0.45	0.22
ρ_{meta}	4.56	4.44	4.04	4.21	4.60	4.77	2.75	3.96
f	0.01	0.04	0.01	0.02	0.02	0.02	0.03	0.03

[a] The substituent is trans unless otherwise states.

[b] These figures were calculated from the data of Spilski and co-workers.[28]

TABLE D-17

Variation of σ_R^{para} and ρ_{meta} with β-Substituent in $CDCl_3$ (Literature data)

Ring substituent	σ_R^{para} for β-substituent[a] Me/Me[24]	H[21]	Ph[24]	4-C_5H_4N[84]	2-C_5H_4N[84]	Fe^+CO[27]	PhCO[26]	NO_2[23]
4-NMe_2	-0.91	-1.25	-1.28	-1.39	-1.45	-1.74	-1.85	-2.03
4-OMe	-0.62	-0.79	-0.79	-0.86	-0.87	-0.98	-0.98	-1.03
4-Me	-0.16	-0.24	-0.25	-0.24	-0.26	-0.31	-0.28	-0.29
4-F	-0.57	-.062	-0.59	-0.58	-0.62	-0.55	-0.66	-0.62
4-Cl	-0.28	-0.31	-0.30	-0.34	-0.32	-0.36	-0.35	-0.35
4-Br	-0.23	-0.27	-0.27	-0.28	-0.28	-0.31	-0.28	-0.31
4-CN	-	0.30	0.29	-	-	0.22	-	0.23
4-NO_2	-	0.44	0.49	0.33	0.48	0.49	0.51	0.28
ρ_{meta}	4.17	4.13	3.86	3.96	3.49	3.20	3.16	2.74
f	0.01	0.02	0.01	0.03	0.03	0.04	0.03	0.07

[a] The β-Substituent is trans- to the aryl group.

This ranking is independent of the ring substituent. Anomalies are relatively minor and can normally be accounted for in terms of experimental error. For the case of a single <u>trans</u>- β- substituent the observed order is $-Br \simeq -H \simeq -Ph < 4\text{-}C_5H_4N < 2\text{-}C_5H_4N < -CO_2Me < CN \simeq MeSO_2 \simeq OCFe^+ < PhCO < Ac \simeq NO_2$

This ranking order is consistent with some sort of dependence on the resonance withdrawing ability of the β- substituent. The most widely accepted scale for quantifying the withdrawing ability of resonance electron withdrawing substituents is the σ_R^- scale of Ehrenson, Brownlee and Taft. The σ_R^- values available for the β- substituents of this study are:

Substituent:	Br	H	C_6H_5	CO_2Me	CN	$MeSO_2$	Ac	NO_2
σ_R^- :	-0.19	0	0.04	0.34	0.33	0.38	0.47	0.46

This is qualitatively very similar to our ranking order for the β-substituents but unfortunately, quantitatively the relationship is only approximate. This may be due to a number of factors. For example the σ_R^- values listed are for use in protic solvents while these $^{13}C_\beta$ SCS's were recorded in deuterochloroform and it was noted earlier that <u>para</u>- substituent effects are not independent of solvent. Another factor may be that although these β- substituent effects are clearly strongly dominated by resonance effects, there is no reason to expect them to be entirely independent of the inductive nature of the β- substituent (although the similarities in the effects of H and Br and Ac and NO_2 suggests inductive effects are

unimportant). Also σ_R^- is just one commonly used point on a possible sliding scale of resonance substituent effects.

On the assumption that there is a relationship between σ_R^- for the β-substituents and the σ_R values for the resonance donating ring substituents, it is possible to estimate σ_R^- values for those β-substituents not on Ehrenson, Brownlee and Taft's list. For example, the 2- and 4-pyridyl groups on this basis, should have σ_R^- about midway between that of the phenyl group (0.04) and that of the carbomethoxy group (0.34). Thus σ_R^- for these groups should be around 0.2 - 0.3. Unfortunately σ_I for these groups has not been determined so σ_R^- is unknown.

Happer has compared the σ_R^{para} data for the +R ring substituents for many of the series in table D-17 with Ehrenson, Brownlee and Taft's σ_R scales (σ_R^-, σ_R^o, $\sigma_{R(BA)}$ and σ_R^+) and found that these series generate σ_R values which were between $\sigma_{R(BA)}$ and σ_R^+. The β,β dimethylstyrenes required a scale close to $\sigma_{R(BA)}$ and at the other extreme the β-nitrostyrenes requires a scale close to σ_R^+. A similar comparison with the series prepared in this study (see Table D-16) shows that they lie in the same range. Ehrenson, Brownlee and Taft's σ_R^o, $\sigma_{R(BA)}$ and σ_R^+ for our series of <u>para</u> +R substituents are listed below.

	H	M_e	OM_e	NMe_2	F	Cl	Br	CN	NO_2
σ_R^o	0.00	-0.11	-0.45	-0.52	-0.34	-0.23	-0.19	0.13	0.15
$\sigma_{R(BA)}$	0.00	-0.11	-0.61	-0.83	-0.45	-0.23	-0.19	0.13	0.15
σ_R	0.00	-0.25	-1.02	-1.75	-0.57	-0.36	-0.30	0.13	0.15

It appears that a series corresponding to σ_R^o would require a strong electron donating β-substituent.

Happer related the apparent σ_R scales of each of the β-substitued styrene series to the "electron demand" of the side-chain. Thus another way of looking at the β-substituents of the current study would be to say that they induce electron demands which are between that of reactions which require $\sigma_{R(BA)}$ and that of reactions which require σ_R^+.

3.2 Cis-β AND β,β-DISUBSTITUTED- SUBSTITUENT EFFECTS

The analysis so far has essentially only dealt with those β-substituted styrenes which have the β-substituent trans- to the aromatic ring. If the data for the cis- and trans- β-bromostyrenes is compared it is evident that the β-substituent in the cis-position has a different effect to the same substituent in the trans-position. This is probably due to the steric requirement of the cis-β-substituent slightly affecting the coplanarity of the ring and side-chain. However, the results for the cis- and trans- cinnamonitriles do not significantly differ from one another when we would expect to see an effect similar to that observed with the β-bromostyrenes. It is possible that the much greater resonance interaction occurring with a β-cyano substituent helps to maintain the coplanarity of the ring and side-chain and so preserves the same extent of resonance in both the cis- and trans- cinnamonitriles.

The β,β-disubstituted styrenes should also show similar effects since in these derivatives one of the two substituents must inevitably be cis- to the aromatic ring. The only series of this type prepared in this study are the methylsulphonyl esters, but literature data available for comparison include those for the β,β-dimethylstyrenes, β,β-dichlorostyrenes, and β,β-diacetylstyrenes. Calculated σ_R^{para} values for these substituents are shown in Table D-18.

The values for the β,β-dichloro series must be less reliable than the others because the value of ρ for this series is very uncertain. Either the m-NO_2 or the m-Cl $^{13}C_\beta$ SCS must be in error. We have assumed it to be the former because (a) in other series nitro-substituted derivatives have been shown to give significantly solvent dependent C_β shifts and (b) the assumption leads to a much more consistent set of σ_R^{para} values.

Comparisons with series bearing only one β-substituent are not easy but some trends can be observed. If one assumes that Cl and Br behave in a similar fashion as β-substituents, then the indications are that the earlier observation that the introduction of a halogen into the β-position had little influence on σ_R for +R substituents can be extended to conclude that even adding a second β-substituent makes little difference. If we now turn to the β-acetyl substituted derivatives it can been seen that here the introduction of a second acetyl group, if anything decreases the extent of interaction between para- +R

TABLE D-18

Variation of σ_R^{para} and ρ_{meta} with β-Substituents in β,β-Disubstituted Styrenes in $CDCl_3$

	σ_R^{para} in series			
Ring Substituents	Me,Me[24]	Cl,Cl[30]	Ac,Ac[31]	$MeSO_2$,CO_2Et
4-NMe_2	-0.91		-1.73	-2.18
4-OMe	-0.62	-0.79	-0.93	-1.06
4-Me	-0.16	-0.21	-0.25	-0.32
4-F	-0.57		-0.49	-0.61
4-Cl	-0.28	-0.30	-0.32	-0.34
4-Br	-0.23		-0.25	-0.34
4-CN		0.15	0.11	
4-NO_2	0.22[a]	0.27	0.16	0.22
ρ_{meta}	4.17	4.41	3.16	3.96
f	0.01	0.06	0.01	0.03

[a] Value for CCl_4.

substituents and the side-chain. This suggests that not only is the second acetyl unable to interact with the +R substituent, implying that it is not coplanar with the ethenyl group, but that it may also be slightly upsetting the coplanarity of the system as a whole.

In contrast to both these observations, however, it may be noted that in the series where the β-carbon has both a carboethoxy and a methylsulphonyl group bonded to it, the degree of interaction with para- +R substituents is greater than the case of either the methyl cinnamates or the styryl sulphones. The problem of additivity of B-substituent effects clearly warrants further investigation.

3.3 THE EFFECT OF THE β-SUBSTITUENT ON σ_R^{para} FOR THE -R RING SUBSTITUENTS

The SCS's for the para- resonance electron withdrawing substituents (for example p-NO_2) are difficult to interpret because few are included in this investigation. An inspection of Tables D-16 and D-17 shows that σ_R^{para} for these substituents is not simply the reverse of that for the para- resonance donors. The three factors which could influence σ_R^{para} for the -R substituents are the inductive effect of the β-substituent, the resonance effect of the β-substituent, and the steric effect in the case of cis-β-substituents. For para-nitro-, which is the -R substituent for which most data are available, most series fall into three groups. There is a group for which σ_R^{para}

is about 0.5, which is about the value of σ_R^- for the $-NO_2$ group. The members of this group are the series with β-substituents C_6H_5CO, Fe^+CO, C_6H_5 and $2\text{-}C_5H_4N$. These β-substituents appear to have very little in common. The second group with $\sigma_R^{para} \simeq +0.45$ contains the series with β-substituents H, CO_2Me, and Ac. These substituents also seem to have little in common. Finally there are the rest of the series and these for the most part have σ_R^{para}'s for the nitro-substituent of +0.30 or less. This group includes such varied β-substituents as Br(cis), CN(cis- and trans-), $4\text{-}C_5H_4N$ and NO_2. If we can make any broad generalisations at all about these results it is that the higher values of σ_R^{para} for the $-NO_2$ group appear to be associated with the weaker inductive electron withdrawing β-substituents (such as the carbonyl derivatives, H, and phenyl) and perhaps +R β-substituents. Lower σ_R^{para} values are found for the strongly inductive electron withdrawing β-substituents. It is interesting to note, that just as was the case for +R groups, lower values are also associated with series where at least one β-substituent is cis- to the aromatic ring. The situation clearly warrants further investigation using a greater variety of -R para- substituents and +R β- substituents.

3.4 THE EFFECT OF THE β- SUBSTITUENT ON ρ_{meta}

The values of ρ_{meta} corresponding to the different β-substituents are listed in Tables D-16 and D-17. They show small but distinct changes over the range of

β- substituents. One remarkable feature is that the β- substituents with high potential for resonance interaction with +R ring substituents; that is the series β-Ac, β-PhCo, β-$Fe^{+}CO$ and β-NO_2; apparently induce a depressed ρ_{meta} value. We would have expected ρ_{meta} for these β- substituents to have been higher than the norm since the system would be expected to be more sensitive to changes in substituent. There is no obvious explanation for the observed trends.

3.5 THE EFFECT OF SOLVENT ON σ_R^{para}

A detailed study of the solvent dependence of σ_R^{para} is beyond the scope of this thesis but the subject does warrant the following brief discussion.

All of the data given in Tables D-16 and D-17 were measured in deuterochloroform solution. It would be useful to have this data recorded in other solvents and in particular ethanol. However, many of the derivatives would be insufficiently soluble in ethanol to obtain satisfactory spectra. The only series for which data recorded in a variety of solvents, are available for para- substituents is the styrenes themselves. The effect of solvent on σ_R^{para} in the styrenes is summarised in Table D-19. It can be seen from the table that differences are in general small but that the σ_R^{para} values in ethanol or 75% ethanol are smaller in magnitude than those values in $CDCl_3$ particularly for the important +R ring substituents. As noted earlier, the β,β-dimethylstyrene

TABLE D-19

The Effect of Solvent on σ_R^{para} in the Styrenes

	σ_R^{para} in						
Substituent	75% EtOH	EtOH	Me_2SO	Me_2CO	$CDCl_3$	CCl_4	C_6H_6
NMe_2	-	-	-1.19	-	-1.25	-1.13	-
OMe	-0.72	-0.72	-0.76	-0.74	-0.79	-0.74	-0.81
Me	-0.21	-0.23	-0.22	-0.20	-0.24	-0.22	-0.25
F	-0.56	-0.58	-0.57	-0.56	-0.62	-0.58	-0.64
Cl	-0.26	-0.27	-0.28	-0.28	-0.31	-0.29	-0.32
Br	-0.23	-0.25	-0.25	-0.25	-0.27	-0.25	-0.28
CF_3	0.22	0.22	0.21	0.18	0.22	0.20	0.22
CN	0.31	0.28	0.29	0.27	0.30	0.25	0.27
NO_2	0.42	0.39	0.44	0.39	0.44	0.35	0.40

series generates a scale of σ_R which is very similar to σ_R^{BA}. However, the σ_R values thus generated for the halogeno substituents are a little too negative. If allowance is made for the significant solvent effect on σ_R^{para} for these substituents in moving from 75% aqueous ethanol to $CDCl_3$ (see Table D-19) then these values look much more reasonable. Since the DSP σ_R scales were derived for systems in aqueous or mixed aqueous-organic solvents, the solvent effect on σ_R is great enough to effect the ability of the DSP equation to correlate data in solvents such as $CDCl_3$.

3.6 THE EFFECT OF THE β-SUBSTITUENT ON $^{13}C_\alpha$ SCS's

As was noted earlier, the $^{13}C_\alpha$ SCS become available as a by-product of the primary study involving $^{13}C_\beta$ shifts. The $^{13}C_\alpha$ SCS's obtained for all the series in this study are therefore presented in Table D-20 and the C_α data corresponding to the C_β data of Table D-17 are reproduced here in Table D-21. The possible origin for the reversed order of $^{13}C_\alpha$ substituent effects was touched upon in section 1.2. It is possible that examination of the $^{13}C_\alpha$ SCS's for series of compounds for which the β-substituent is systematically varied might shed some further light on their origin.

Unlike the situation with the C_β data, the $^{13}C_\alpha$ SCS's for the <u>meta</u>- substituted derivatives are not linearly related to one another and to σ^{meta} but vary with the nature of the β- substituent. Thus the method of analysis

TABLE D-20

$^{13}C_{\alpha}$ Substituent Chemical Shifts* for β-Substituted Styrenes

(Current Investigation)

Ring Substituent	β-Substituent							
	Br	Br(cis)	CO_2Me	CN	CN(cis)	$MeSO_2$	Ac	$MeSO_2/CO_2Et$
3-CH_3	0.11	0.13	0.28	0.22	0.15	0.15	0.20	0.08
3-OCH_3	-0.08	-0.15	-0.06	-0.03	0.00	-0.11	-0.07	-0.24
3-F	-0.99	-0.96	-1.39	-1.35	-1.39	-1.47	-1.57	-1.55
3-Cl	-1.31	-1.20	-1.66	-1.58	-1.61	-1.65	-1.91	-1.62
3-Br	-1.30	-1.13	-1.77	-1.72	-1.75	-1.80	-1.99	-1.74
3-CF_3	-1.29	-1.20	-1.80	-1.72	-1.64	-1.84	-2.03	-1.61
3-CN	-2.12	-1.93	-2.80	-2.60	-2.55	-2.83	-3.11	-2.29
3-NO_2	-2.14	-1.96	-2.91	-2.72	-2.62	-2.89	-3.27	-2.62
4-NMe_2	-0.20	-	0.48	-0.01	-0.30	0.9[a]	0.90	1.45
4-OCH_3	-0.56	-0.70	-0.35	-0.51	-0.61	-0.37	-0.23	-0.02
4-CH_3	-0.11	-0.13	0.00	-0.04	-0.07	-0.02	0.10	0.03
4-F	-1.16	-1.08	-1.32	-1.34	-1.35	-1.31	-1.39	-1.06
4-Cl	-1.21	-1.11	-1.61	-1.44	-1.44	-1.40	-1.61	-1.27
4-Br	-1.14	-1.04	-1.41	-1.37	-1.30	-1.34	-1.57	-1.20
4-CN	-1.47	-1.39	-2.48			-2.0[a]		
4-NO_2	-1.81	-1.63	-2.99	-2.73	-2.59	-2.4[a]	-3.36	-2.42

a Values taken from reference 28.

* $CDCl_3$ solvent in each case.

TABLE D-21

$^{13}C_{\alpha}$ NMR Substituent Chemical Shifts[a] for β-Substituted Styrenes (Literature Data)

Ring Substituent	β-Substituent									
	Me,Me[24]	H[21]	Ph[24]	4-C_5H_4N[24]	2-C_5N_4N[84]	$OCFe^{+}$[27]	OCPh[26]	NO_2[23]	Cl,Cl[30]	Ac,Ac[31]
3-CH_3	0.08	0.06	0.14	-0.06	0.20		0.24	0.34	0.4	
3-OCH_3	-0.02	-0.07		-0.16	-0.11	-0.18	-0.06	0.09	0.2	
3-F	-0.86	-1.08	-1.17	-1.36	-1.07			-1.22		
3-Cl	-1.18	-1.30	-1.48	-1.57	-1.52	-1.74	-1.71	-1.46	-1.2	-1.7
3-Br	-1.28	-1.40	-1.56	-1.76	-1.71	-1.74	-1.79	-1.66		
3-CF_3		-1.23	-1.54	-1.66	-1.60		-1.95	-1.65		
3-CN		-2.05						-2.67		
3-NO_2	-3.44	-2.16	-2.61	-2.09	-2.65	-2.91	-3.21	-2.57	-1.9	-2.9
4-NMe_2	-0.25	-0.36	0.17	0.12	0.20	0.79	1.13	1.32		1.4
4-OCH_3	-0.55	-0.67	-0.40	-0.20	-0.41	-0.25	0.07	0.13	-0.2	0.0
4-CH_3	-0.11	-0.20	-0.06	-0.19	-0.05	0.01	0.23	0.15	0.1	0.2
4-F	-1.05	-1.20	-1.16	-1.34	-1.26	-1.38	-1.23	-1.05		-1.1
4-Cl	-1.02	-1.22	-1.30	-1.29	-1.42	-1.48	-1.39	-1.23	-1.1	-1.5
4-Br	-1.07	-1.14	-1.29	-1.37	-1.53	-1.35	-1.31	-1.18		-1.3
4-CN		-1.51	-1.93			-2.52		-2.32	-1.3	-2.6
4-NO_2		-1.92	-2.32	-1.97	-2.52	-3.10	-2.93	-2.90	-1.6	-3.1

[a] $CDCl_3$ solvent in each case.

applied to the C_β data is inapplicable here. In section 1.2 the DSP equation was used to analyse C_α data. While the DSP analyses were able to indicate that predominantly inductive effects were operating, the agreement between theory and practice was poor. Similar analyses of the data in Tables D-20 and D-21 gave the same indications of a similar lack of good fit and there was little to be gained by using the analysis for discussion purposes, particularly when both lots of data were deficient in substituents, especially -R ones.

Although we have not found a systematic means adequately analysing $^{13}C_\alpha$ data, a number of comments can be made based on inspection of Tables D-20 and D-21. Firstly, all the C_α data are consistent with shifts being controlled to a large extent by the inductive electronic effects of the ring substituents but the direction of the shifts is the reverse of that observed for C_β and C_{para} (the carbons on either side). This is also the opposite direction to that expected on the basis of normal mechanisms for the operation of inductive effects. A tentative explanation for this has been offered by Brownlee.[20]

Secondly, the existence of reversed resonance effects is indicated at least in the case of +R substituents (consider the p-NMe_2 and p-OMe substituents in Tables D-20 and D-21). These reversed resonance effects are relatively weak but increase with the resonance withdrawing character of the β-substituent. Interestingly these reverse resonance effects are found in both the <u>meta</u>- and the <u>para</u>- series.

Although not listed in Table D-20 the meta- dimethylamino substituent in the methyl cinnamate series is downfield from H- by + 1.14 ppm while the para- dimethylamino- substituent in the same series shows a $^{13}C_{\alpha}$ SCS of only + 0.48.

Finally, there does not seem to be any obvious pattern to the sensitivities of these $^{13}C_{\alpha}$ chemical shifts to changes of ring substituents. However, a comparison with the ρ_{meta} values in Tables D-16 and D-17 suggest that series with highest sensitivities to C_{β} effects (highest ρ_{meta}) have lowest sensitivities to C_{α} effects as gauged by the relative ranges of $^{13}C_{\alpha}$ SCS's amongst the series.

3.7 SUBSTITUENT EFFECTS ON OTHER CARBONS

Reference to the results section of this thesis shows that there is ample scope for discussion of the effect of substituents (and solvents) on the chemical shifts of other carbons present in the various systems. (For example, the para- ring carbons, carbons forming part of the β- substituent group, or even the carbons of the methylene bridges in the XCH_2- substituted methyl cinnamates). However, it was felt that to go into these in any detail was beyond the scope and aim of this thesis.

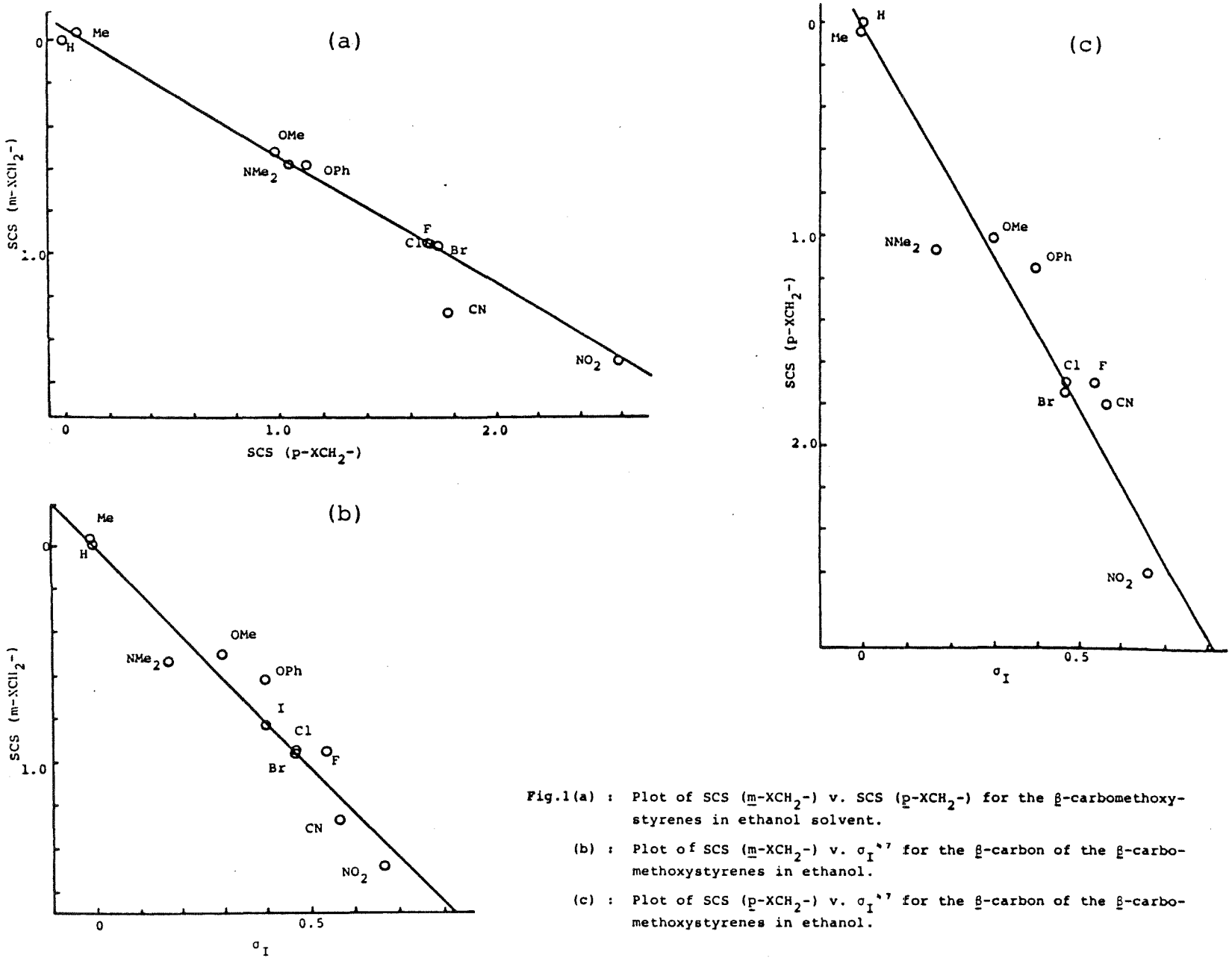
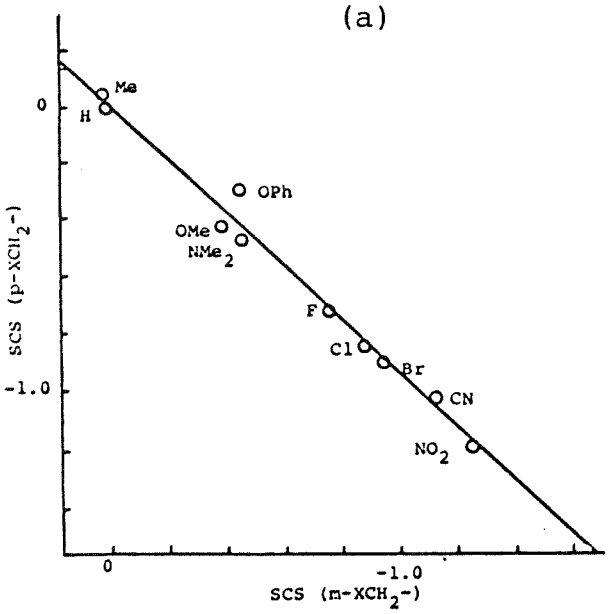


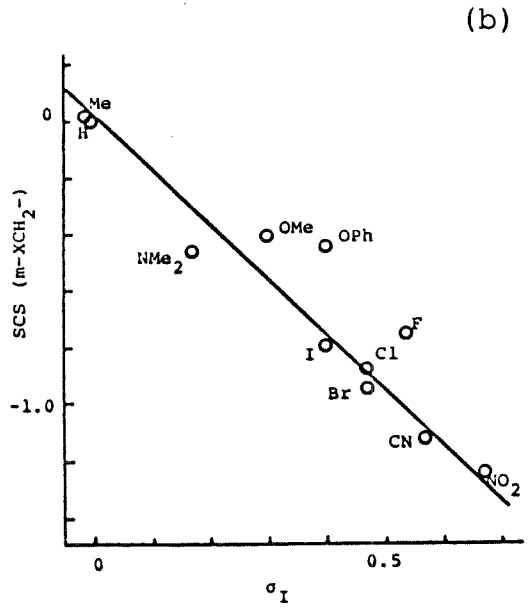
Figure 1

Fig.1(a) : Plot of SCS ($\underline{m}$-XCH_2-) v. SCS ($\underline{p}$-XCH_2-) for the $\underline{\beta}$-carbomethoxystyrenes in ethanol solvent.

(b) : Plot of SCS ($\underline{m}$-XCH_2-) v. $\sigma_I^{\prime\prime}$ for the $\underline{\beta}$-carbon of the $\underline{\beta}$-carbomethoxystyrenes in ethanol.

(c) : Plot of SCS ($\underline{p}$-XCH_2-) v. $\sigma_I^{\prime\prime}$ for the $\underline{\beta}$-carbon of the $\underline{\beta}$-carbomethoxystyrenes in ethanol.





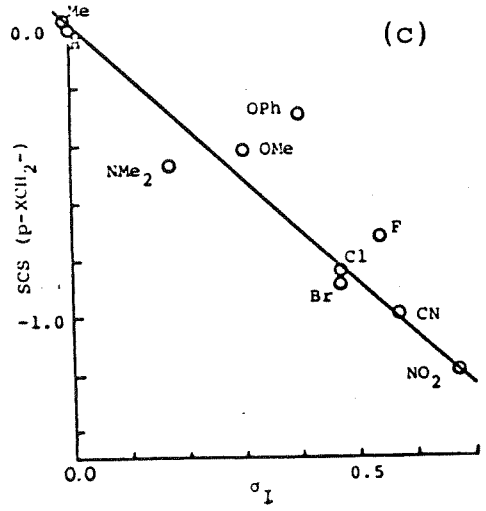


Fig. 2(a) : Plot of SCS (p-XCH_2-) v. SCS (m-XCH_2-) for the α-carbon of the β-carbomethoxystyrenes in ethanol

(b) : Plot of SCS (m-XCH_2-) v. σ_I[67] for the α-carbon of the β-carbomethoxystyrenes in ethanol.

(c) : Plot of SCS (p-XCH_2-) v. σ_I[67] for the α-carbon of the β-carbomethoxystyrenes in ethanol.

Figure 2

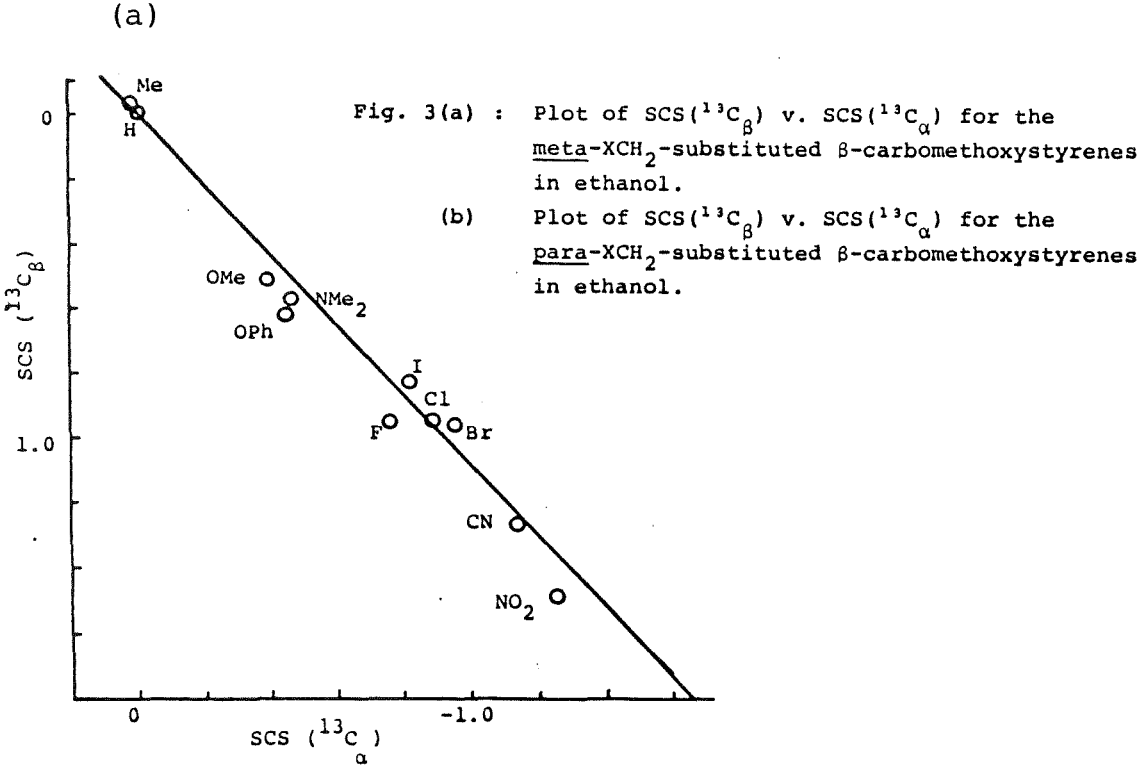


Fig. 3(a) : Plot of SCS($^{13}C_\beta$) v. SCS($^{13}C_\alpha$) for the meta-XCH_2-substituted β-carbomethoxystyrenes in ethanol.

(b) Plot of SCS($^{13}C_\beta$) v. SCS($^{13}C_\alpha$) for the para-XCH_2-substituted β-carbomethoxystyrenes in ethanol.

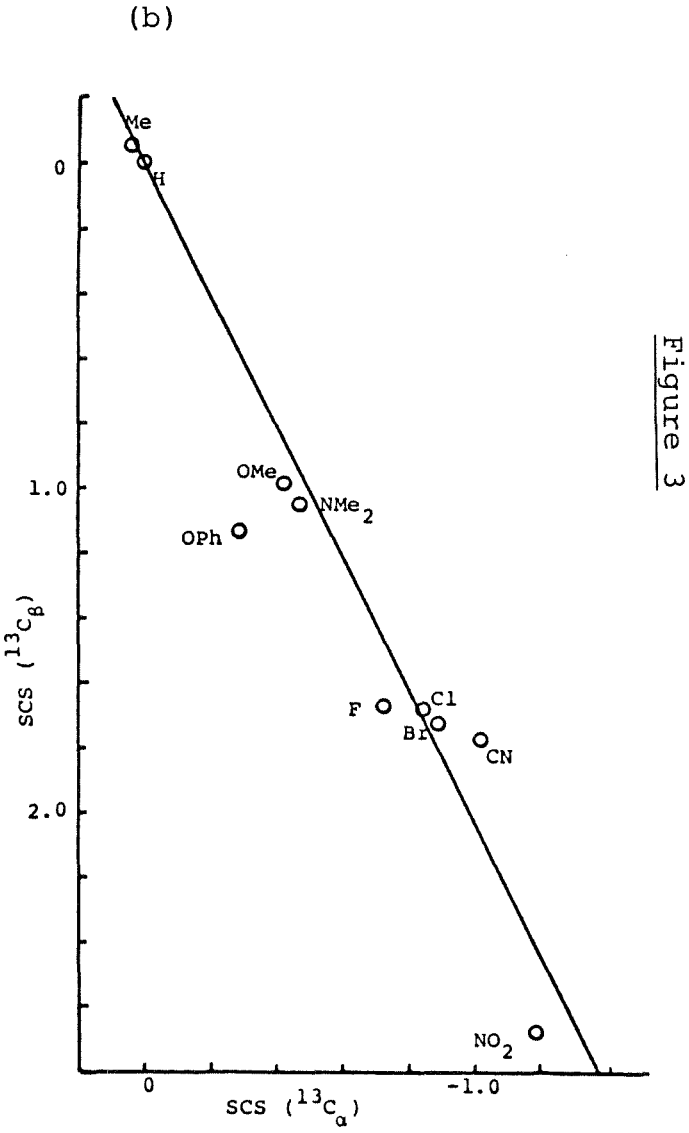


Figure 3

Figure 4

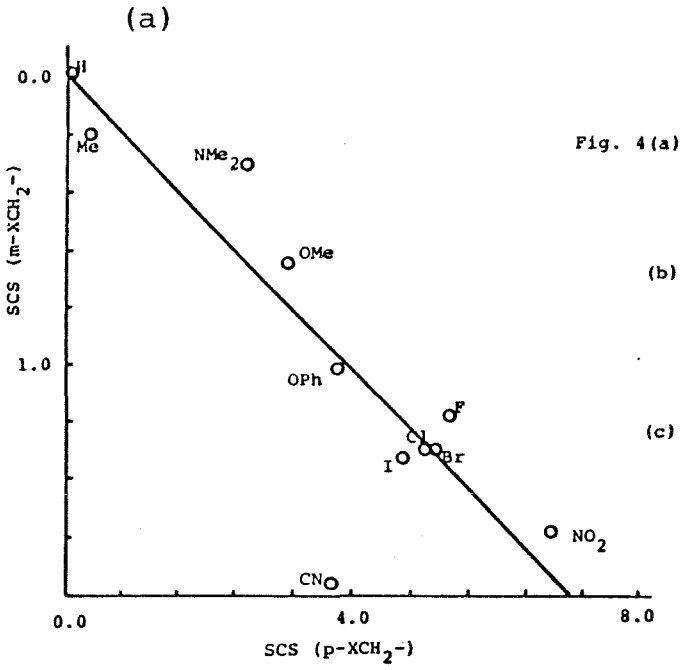
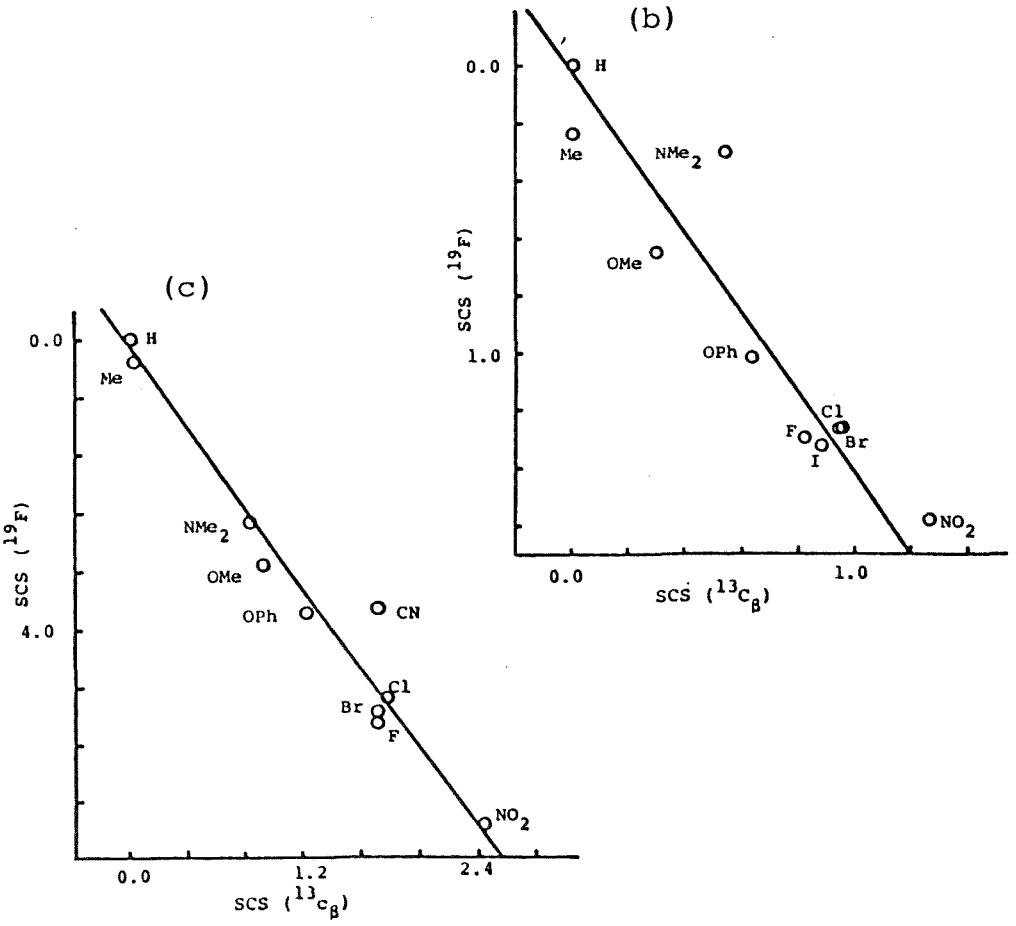


Fig. 4(a) : Plot of ^{19}F SCS (m-XCH_2-) v. ^{19}F SCS (p-XCH_2-) for the XCH_2- substituted fluorobenzenes in acetone solvent.

(b) : Plot of SCS (^{19}F) for the meta-XCH_2- substituted fluorobenzenes v. SCS ($^{13}C_\beta$) for the meta-XCH_2-substituted β-carbomethoxystyrenes in acetone.

(c) : Plot of SCS (^{19}F) for the para-XCH_2-substituted fluorobenzenes v. SCS ($^{13}C_\beta$) for the para-XCH_2-β-carbomethoxystyrenes in acetone.



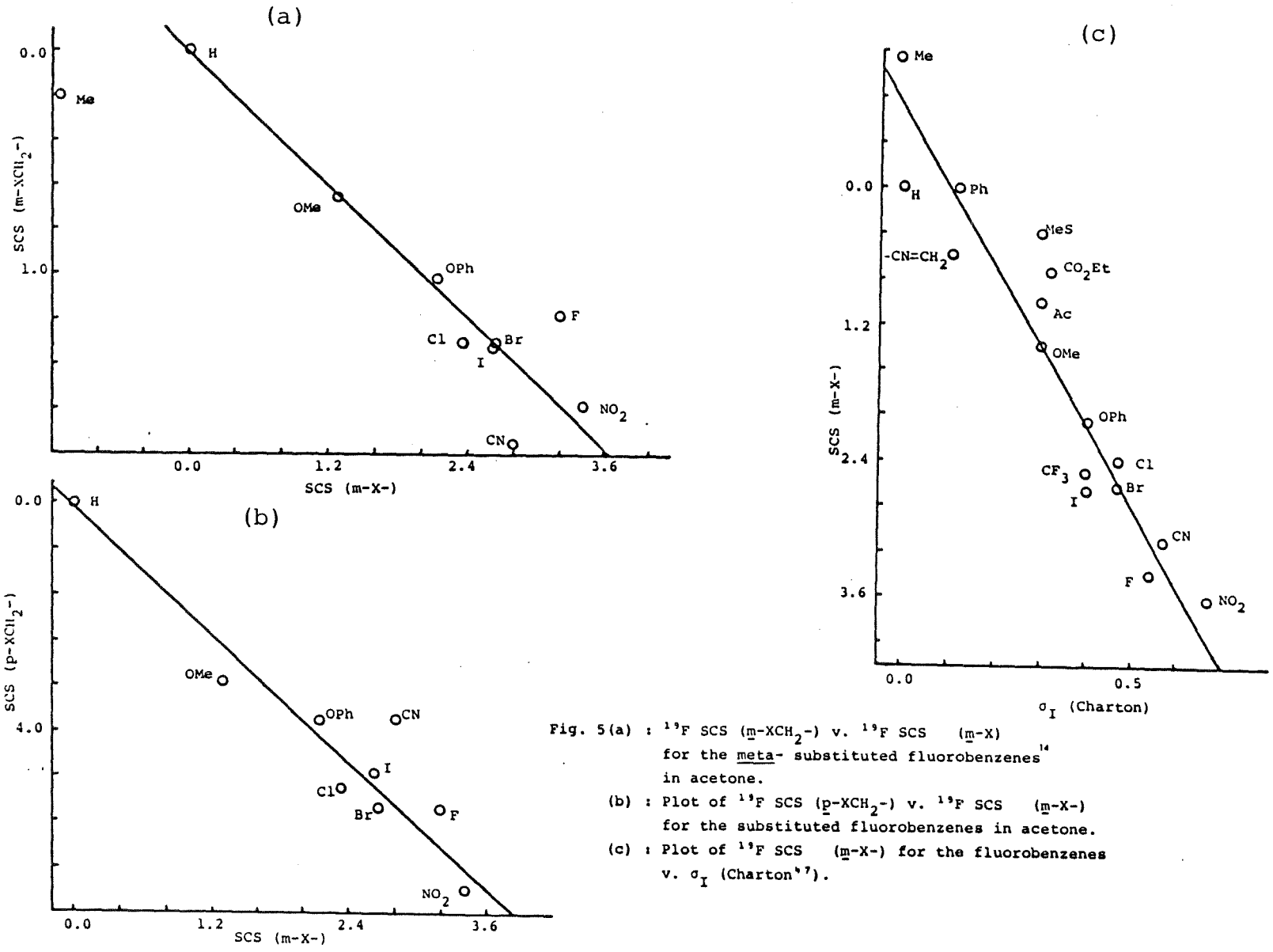


Fig. 5(a) : ^{19}F SCS (m-XCH_2-) v. ^{19}F SCS (m-X) for the meta- substituted fluorobenzenes[14] in acetone.

(b) : Plot of ^{19}F SCS (p-XCH_2-) v. ^{19}F SCS (m-X-) for the substituted fluorobenzenes in acetone.

(c) : Plot of ^{19}F SCS (m-X-) for the fluorobenzenes v. σ_I (Charton[97]).

Figure 5

Figure 6

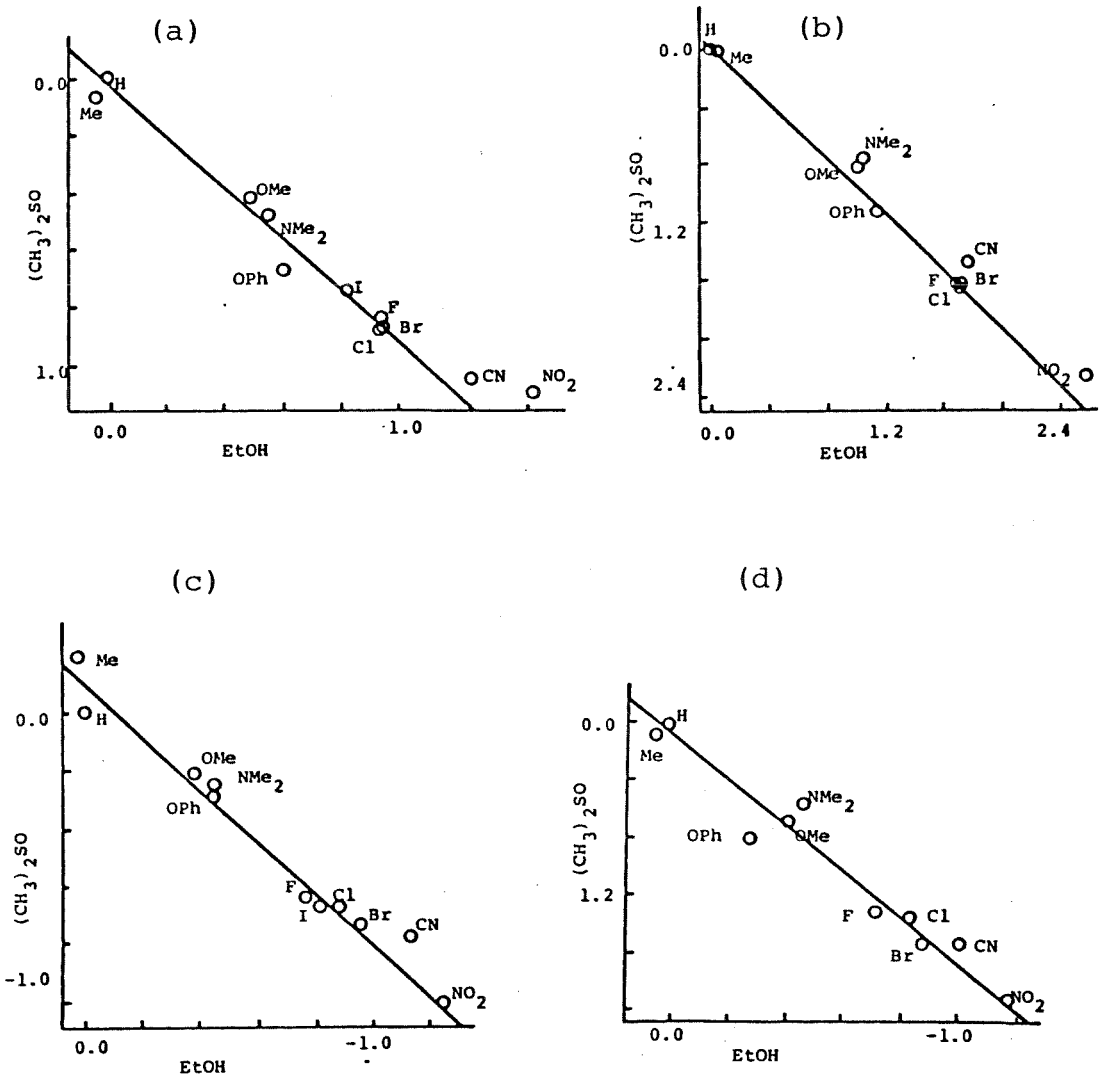


Fig. 6(a) : Plot of SCS ($^{13}C_\beta$) in DMSO v. SCS ($^{13}C_\beta$) in ethanol for the meta-XCH_2- substituted β-carbomethoxystyrenes.

(b) : Plot of SCS ($^{13}C_\beta$) in DMSO v. SCS ($^{13}C_\beta$) in ethanol for the para-XCH_2-substituted β-carbomethoxystyrenes.

(c) : Plot of SCS ($^{13}C_\alpha$) in DMSO v. SCS ($^{13}C_\alpha$) in ethanol for the meta-XCH_2-substituted β-carbomethoxystyrenes.

(d) : Plot of SCS ($^{13}C_\alpha$) in DMSO v. SCS ($^{13}C_\alpha$) in ethanol for the para-XCH_2-substituted β-carbomethoxystyrenes.

Figure 7

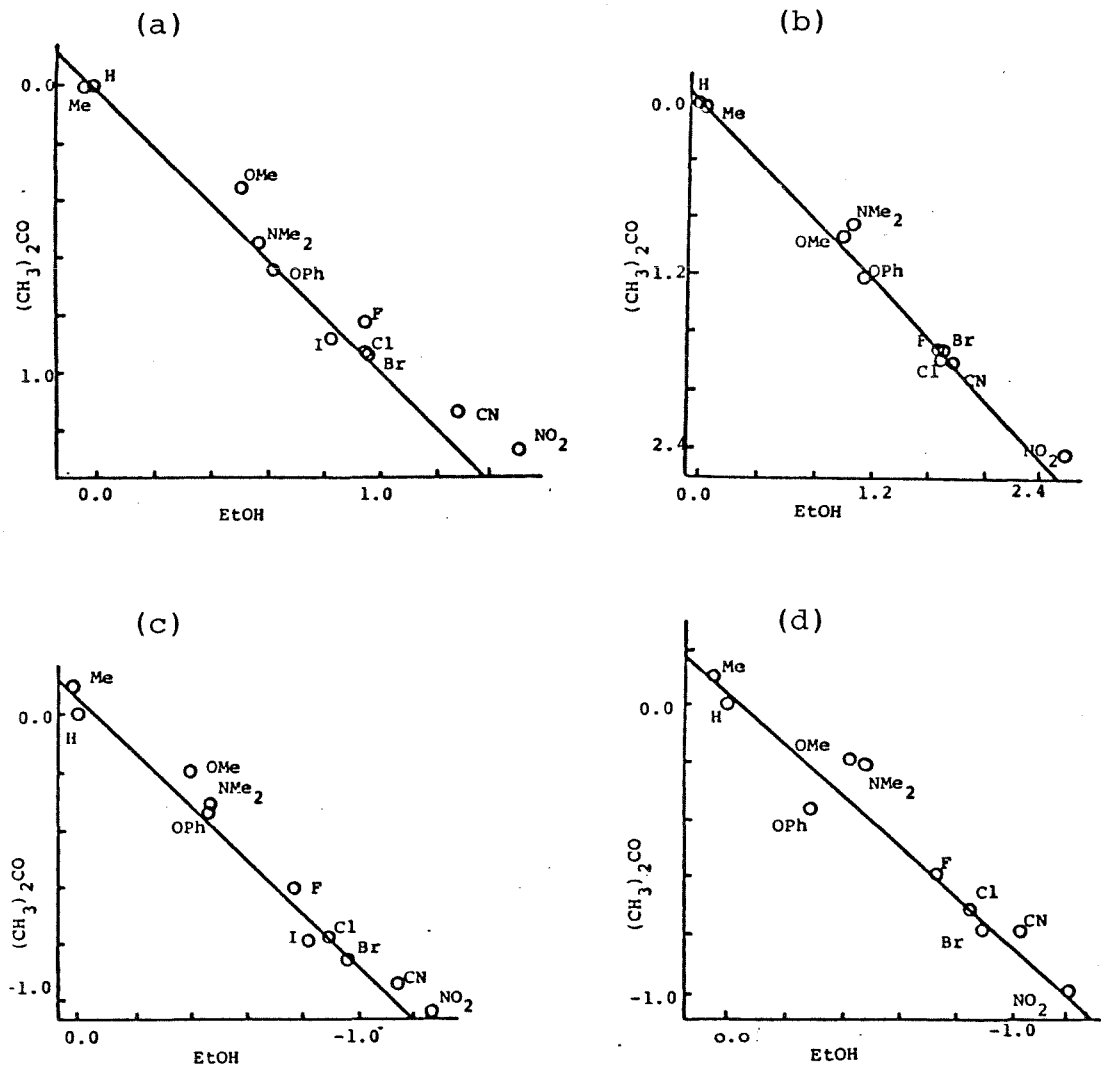


Fig. 7(a) : Plot of SCS ($^{13}C_\beta$) in acetone v. SCS ($^{13}C_\beta$) in ethanol for the meta-XCH_2-substituted β-carbomethoxystyrenes.

(b) : Plot of SCS ($^{13}C_\beta$) in acetone v. SCS ($^{13}C_\beta$) in ethanol for the para-XCH_2-substituted β-carbomethoxystyrenes.

(c) : Plot of SCS ($^{13}C_\alpha$) in acetone v. SCS ($^{13}C_\alpha$) in ethanol for the meta-XCH_2-substituted β-carbomethoxystyrenes.

(d) : Plot of SCS ($^{13}C_\alpha$) in acetone v. SCS ($^{13}C_\alpha$) in ethanol for the para-XCH_2-substituted β-carbomethoxystyrenes.

Figure 8

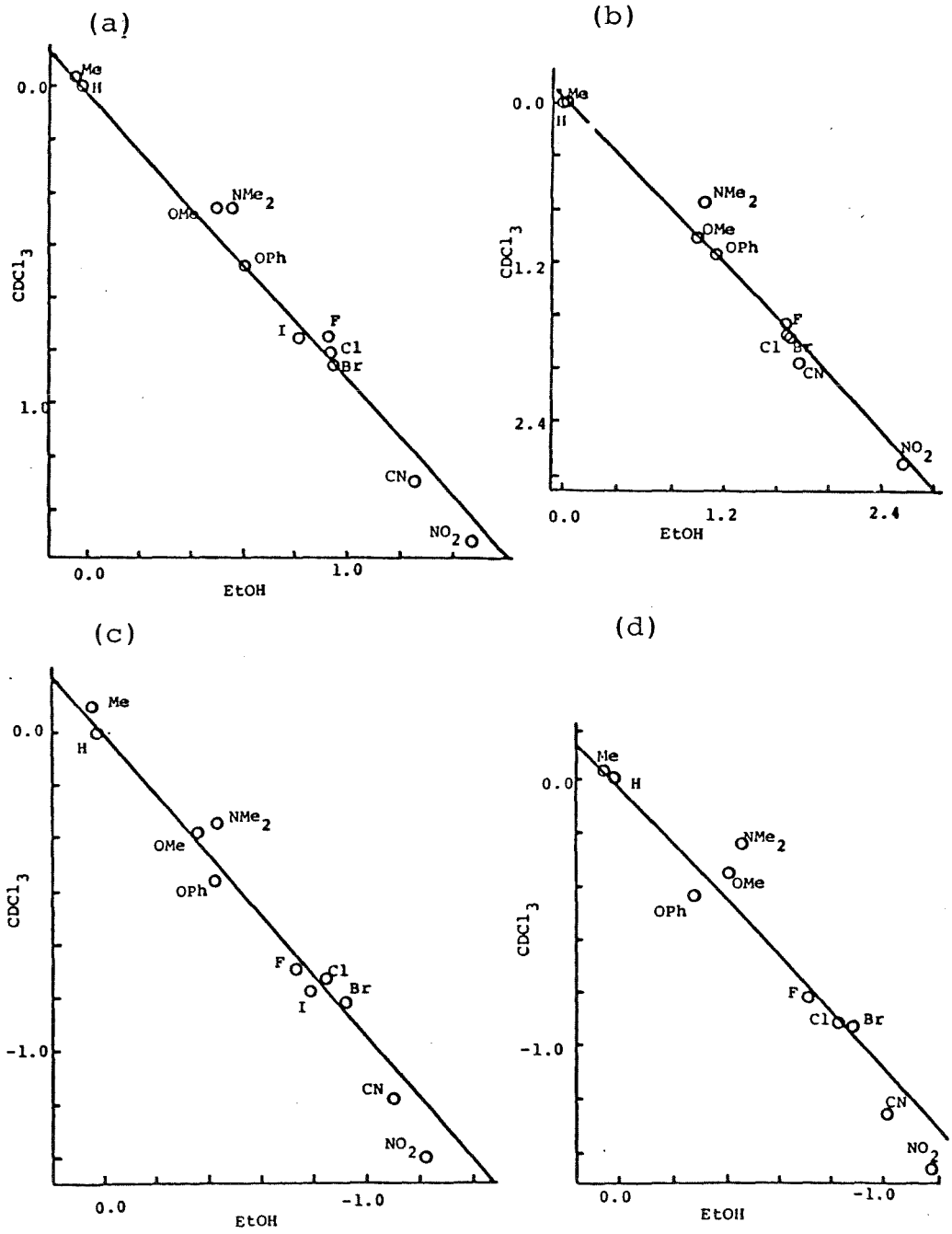


Fig. 8(a) : Plot of SCS ($^{13}C_{\beta}$) in $CDCl_3$ v. SCS ($^{13}C_{\beta}$) in ethanol for the meta-XCH_2-substituted β-carbomethoxystyrenes.

(b) : Plot of SCS ($^{13}C_{\beta}$) in $CDCl_3$ v. SCS ($^{13}C_{\beta}$) in ethanol for the para-XCH_2-substituted β-carbomethoxystyrenes.

(c) : Plot of SCS ($^{13}C_{\alpha}$) in $CDCl_3$ v. SCS ($^{13}C_{\alpha}$) in ethanol for the meta-XCH_2-substituted β-carbomethoxystyrenes.

(d) : Plot of SCS ($^{13}C_{\alpha}$) in $CDCl_3$ v. SCS ($^{13}C_{\alpha}$) in ethanol for the para-XCH_2-substituted β-carbomethoxystyrenes.

Figure 9

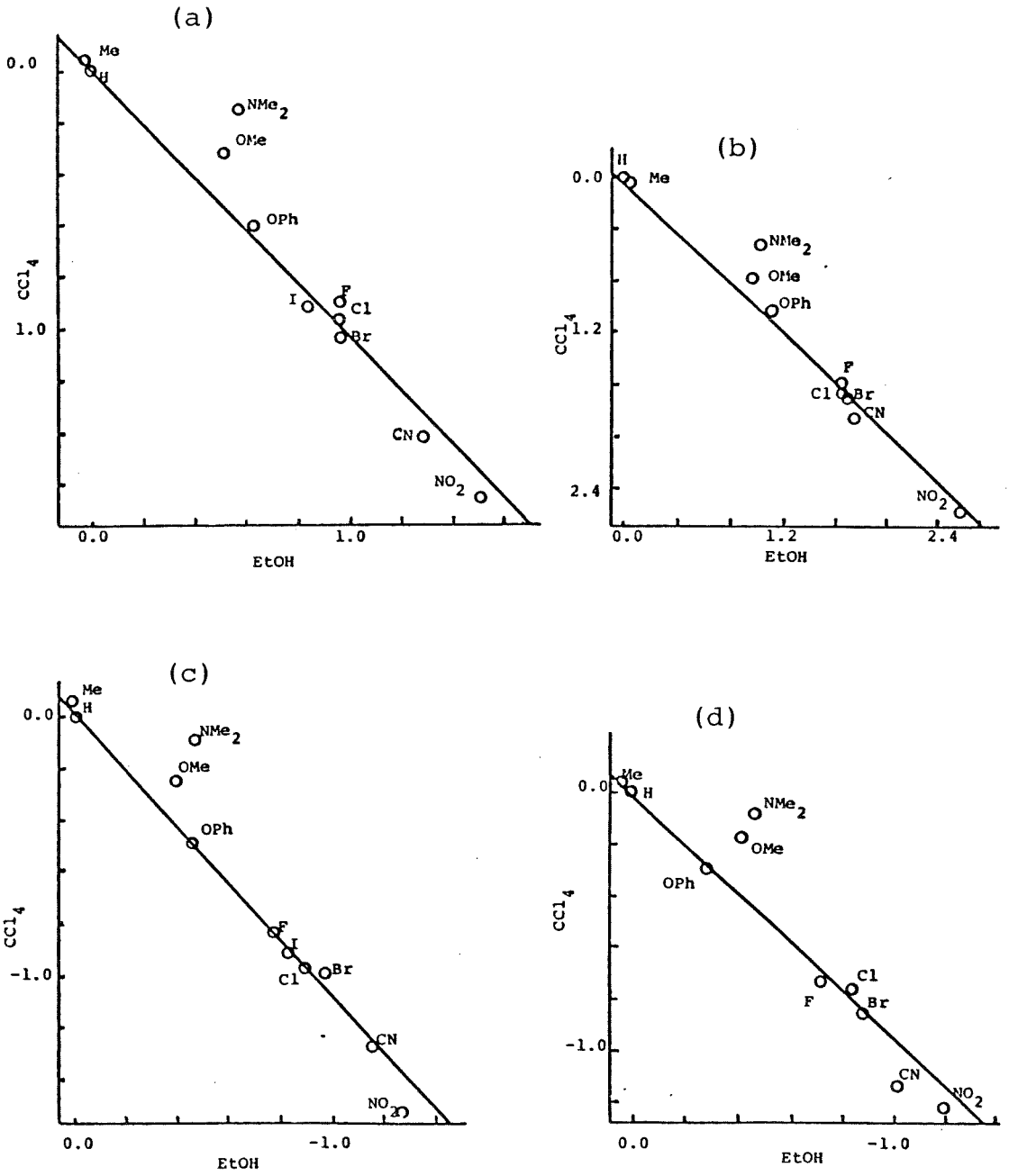


Fig. 9(a) : Plot of SCS ($^{13}C_{\beta}$) for the meta-XCH_2-ß-carbomethoxystyrenes in carbon tetrachloride against the same shifts in ethanol.

(b) : Plot of SCS ($^{13}C_{\beta}$) for the para-XCH_2-ß-carbomethoxystyrenes in carbon tetrachloride against the same shifts in ethanol.

(c) : Plot of SCS ($^{13}C_{\alpha}$) for the meta-XCH_2-ß-carbomethoxystyrenes in carbon tetrachloride against the same shifts in ethanol.

(d) : Plot of SCS ($^{13}C_{\alpha}$) for the para-XCH_2-ß-carbomethoxystyrenes in carbon tetrachloride against the same shifts in ethanol.

Figure 10

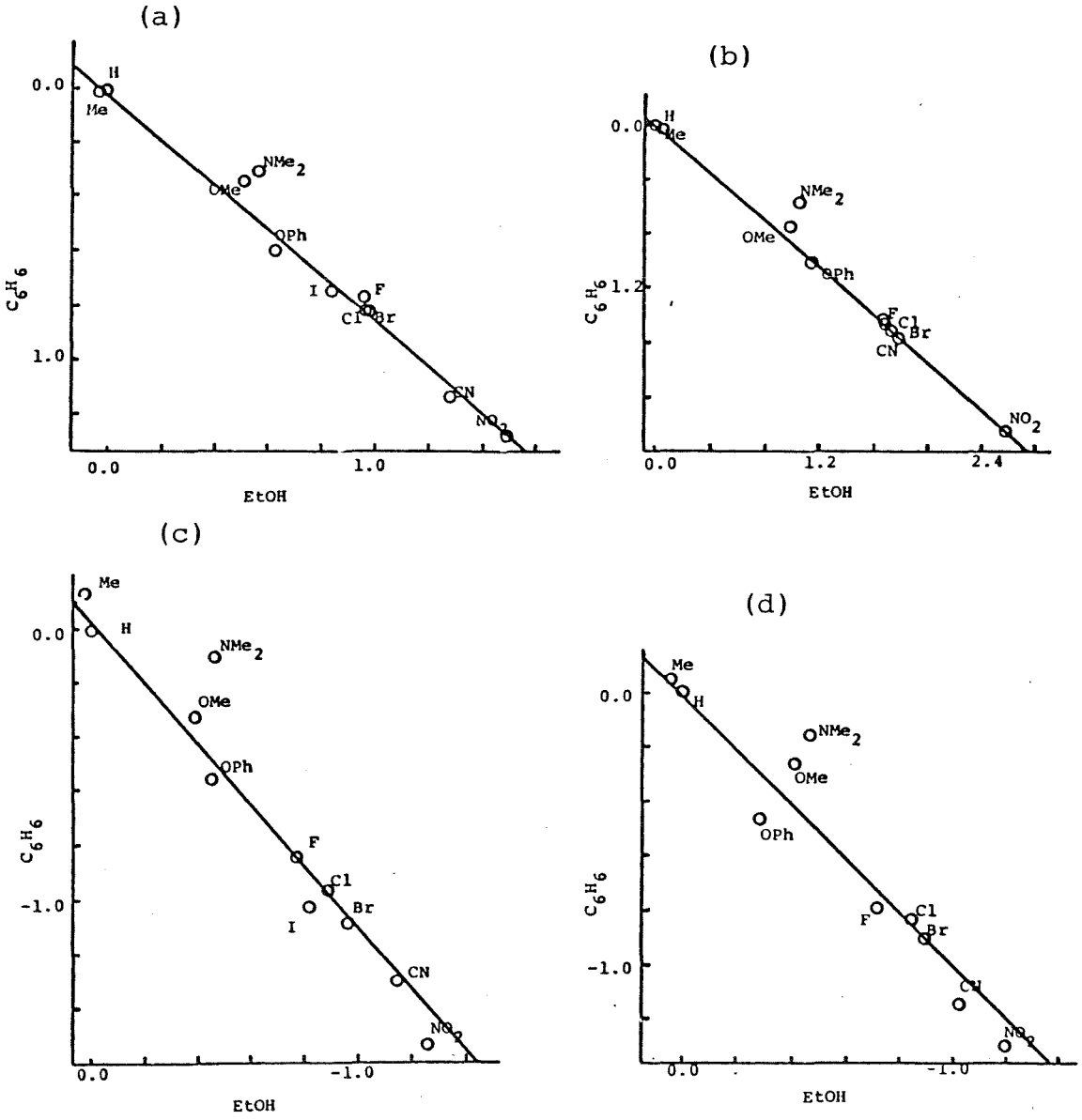


Fig. 10(a) : Plot of SCS ($^{13}C_\beta$) for the meta-XCH_2-β-carbomethoxystyrenes in benzene against the same shifts in ethanol.

(b) : Plot of SCS ($^{13}C_\beta$) for the para-XCH_2-β-carbomethoxystyrenes in benzene against the same shifts in ethanol.

(c) : Plot of SCS ($^{13}C_\alpha$) for the meta-XCH_2-β-carbomethoxystyrenes in benzene against the same shifts in ethanol.

(d) : Plot of SCS ($^{13}C_\alpha$) for the para-XCH_2-β-carbomethoxystyrenes in benzene against the same shifts in ethanol.

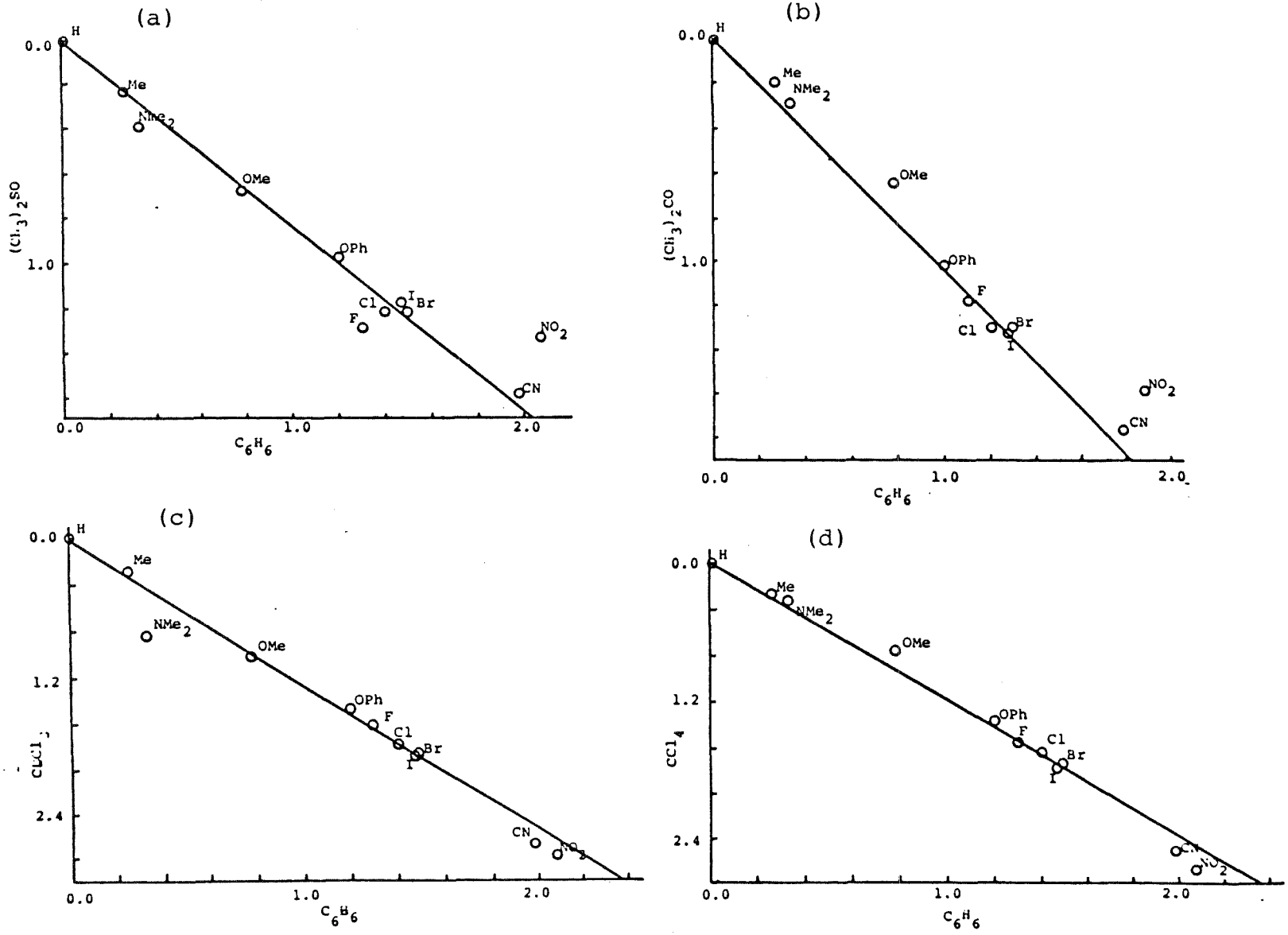


Figure 11

. Fig. 11 : Graphs of SCS (^{19}F) for the meta-XCH_2-substituted fluorobenzenes in the solvents (a) dimethylsulphoxide, (b) acetone, (c) chloroform and (d) carbon tetrachloride against the same shifts in benzene.

Figure 12

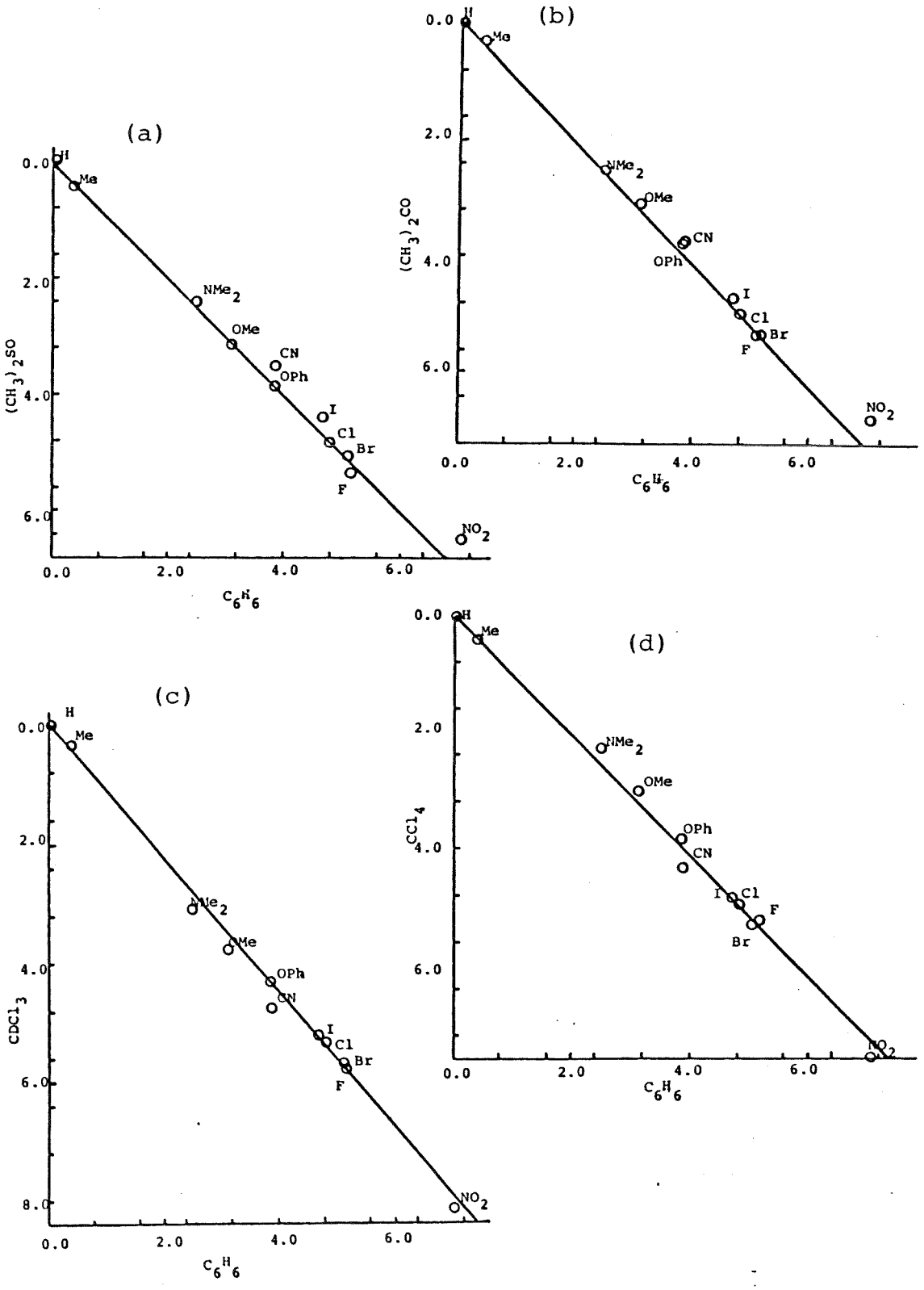


Fig. 12 : Graphs of SCS (^{19}F) for the para-XCH_2-substituted fluorobenzenes in the solvents (a) dimethylsulphoxide, (b) acetone, (c) Chloroform and (d) carbon tetrachloride against the same shifts in benzene.

Table 13

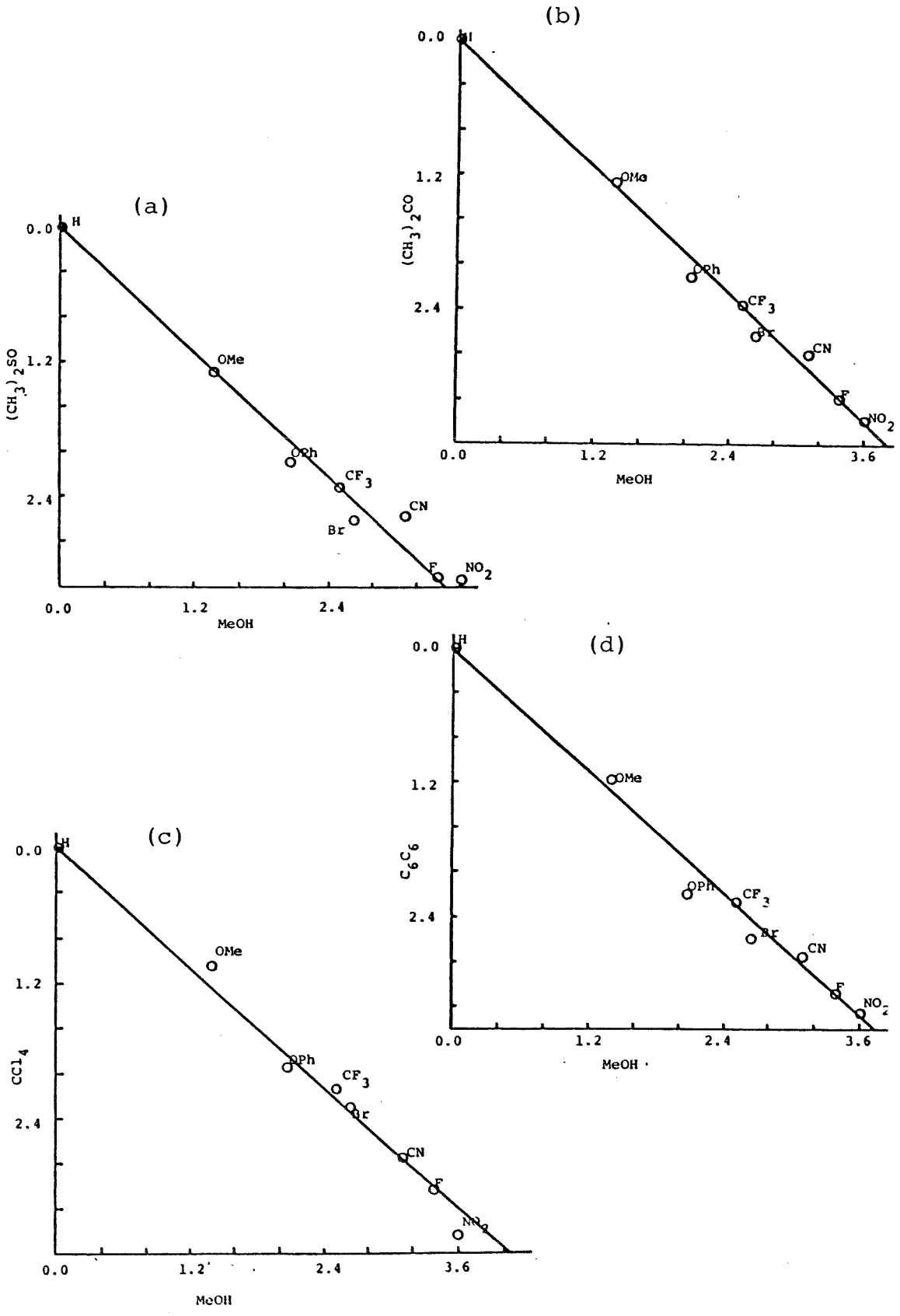


Fig. 13 : Graphs of SCS (^{19}F) for Taft's[1] meta-X-substituted fluorobenzenes in the solvents (a) dimethylsulphoxide, (b) acetone, (c) carbon tetrachloride and (d) benzene against the same data in methanol.

Figure 14

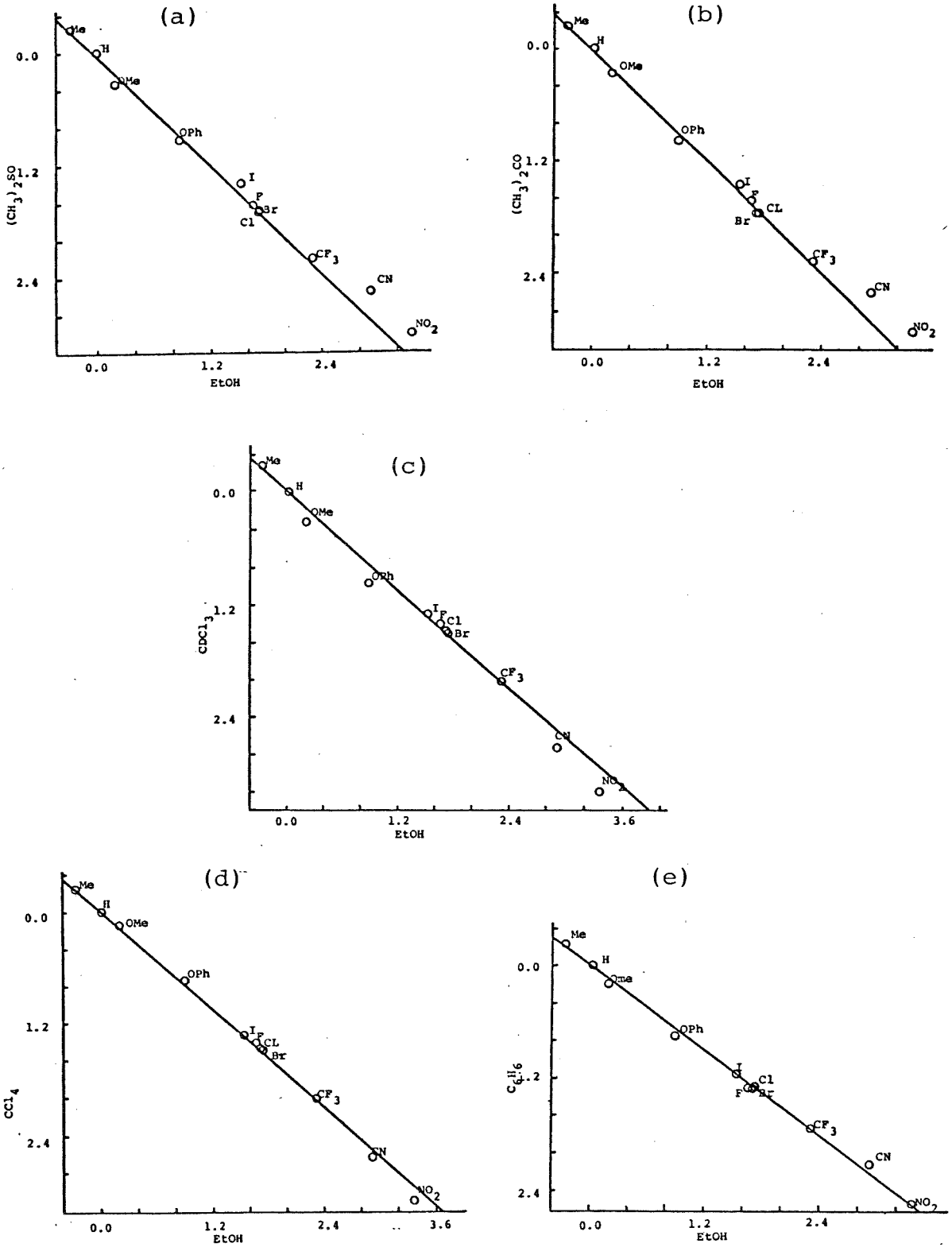


Fig. 14 : Graphs of SCS($^{13}C_\beta$) for the meta-X-substituted β-carbomethoxy-styrenes in solvents

(a) dimethylsulphoxide (b) acetone

(c) deuterochloroform

(d) carbon tetrachloride (e) benzene

against the same data in the solvent ethanol.

Figure 15

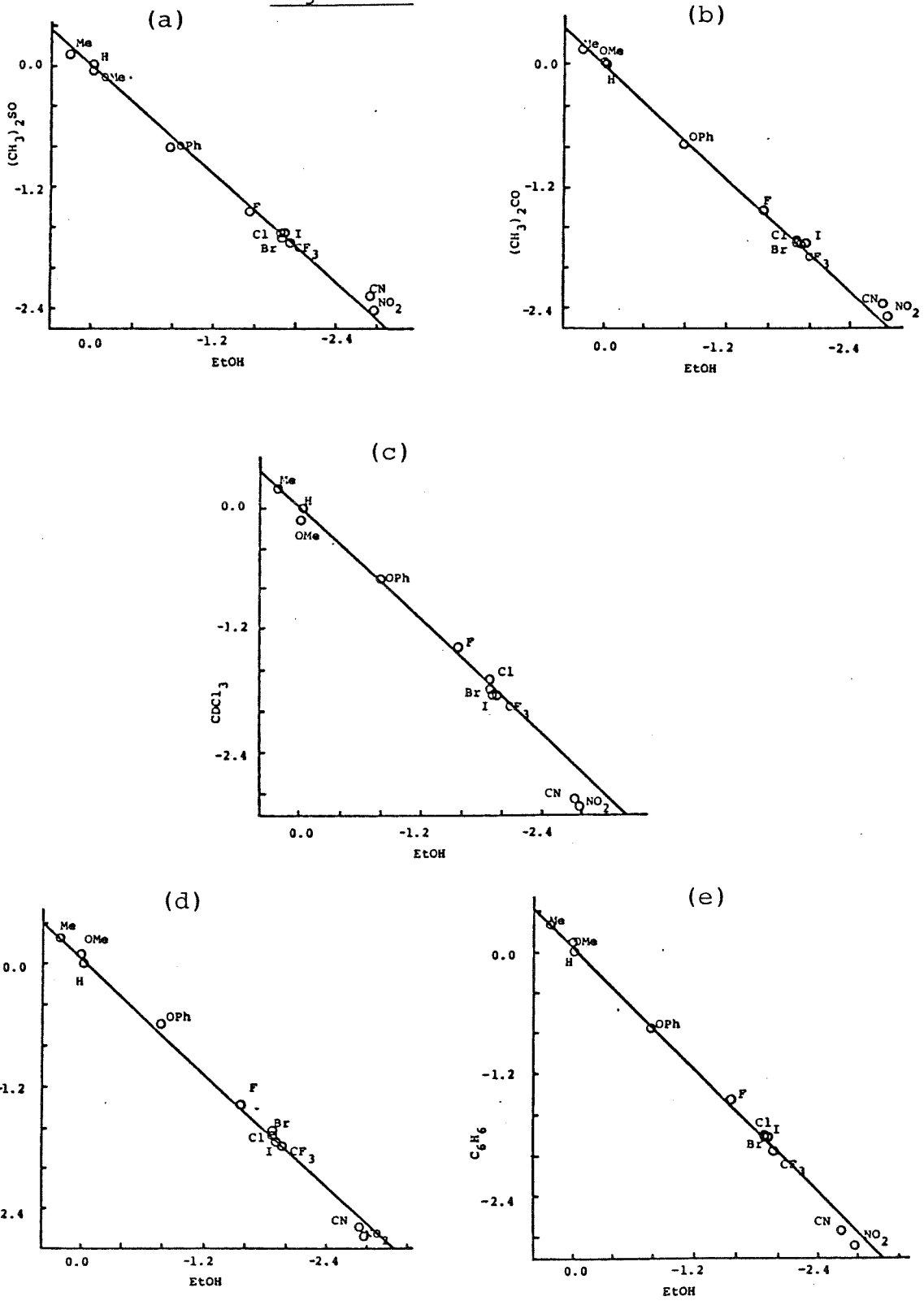


Fig. 15 : Graphs of SCS($^{13}C_\alpha$) for the meta-X-substituted β-carbomethoxy-styrenes in solvents

(a) dimethylsulphoxide (b) acetone

(c) deuterochloroform

(d) carbon tetrachloride (e) benzene

against the same data in the solvent ethanol.

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